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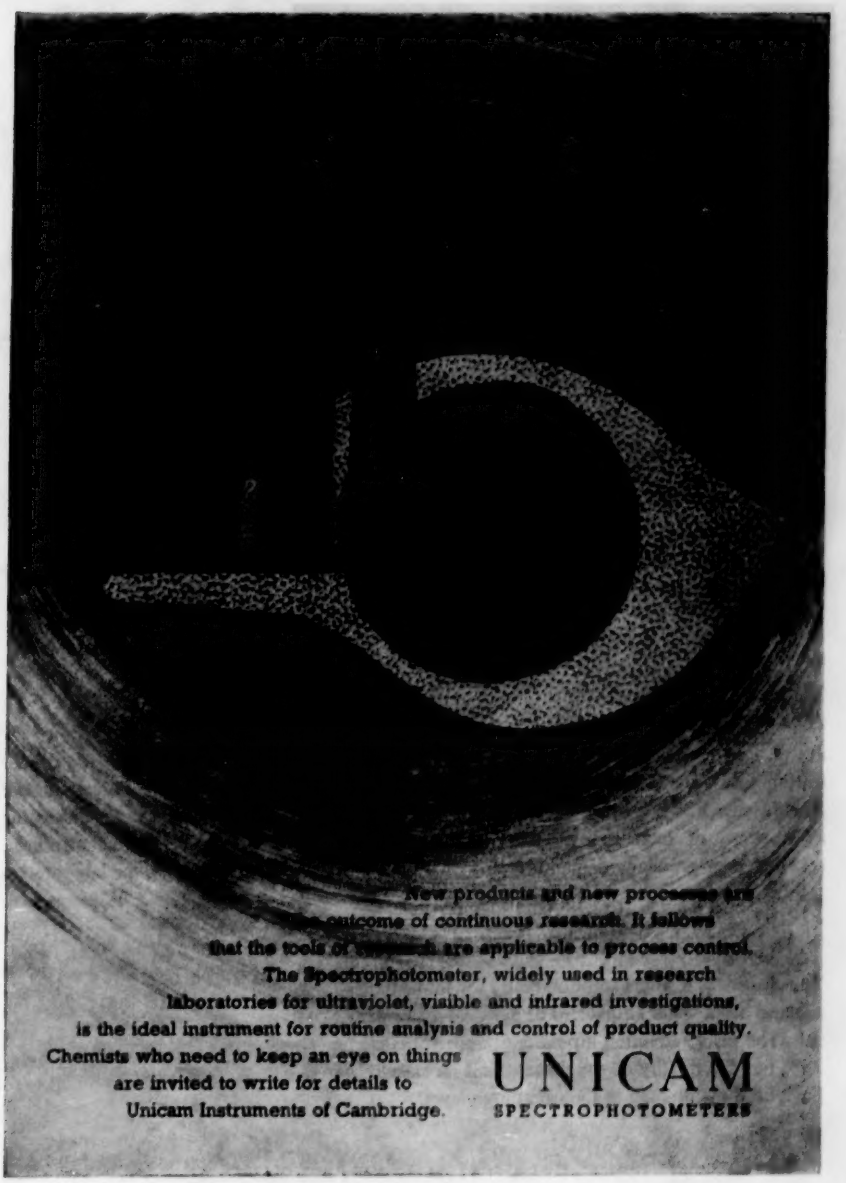
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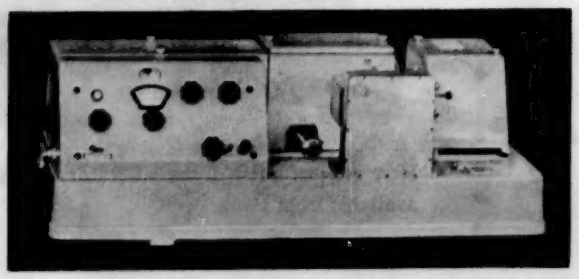

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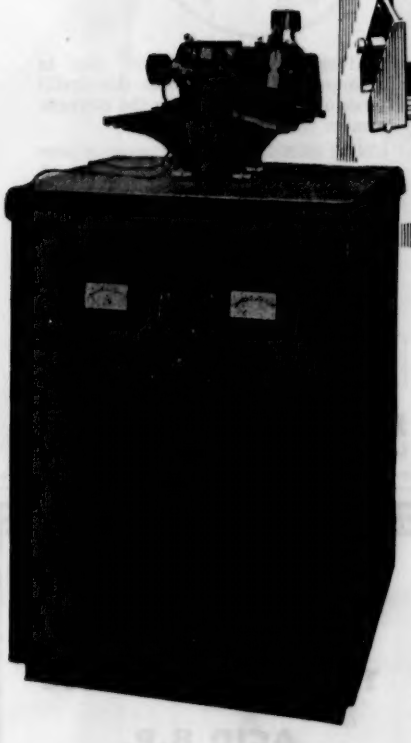

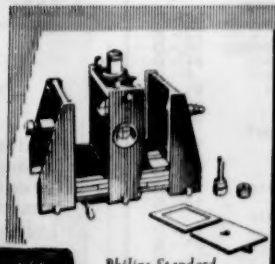

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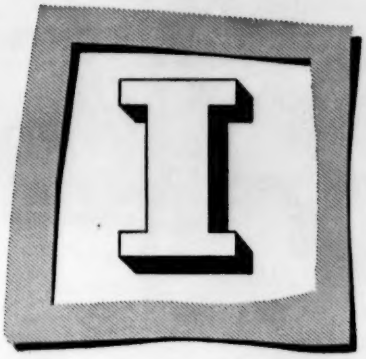

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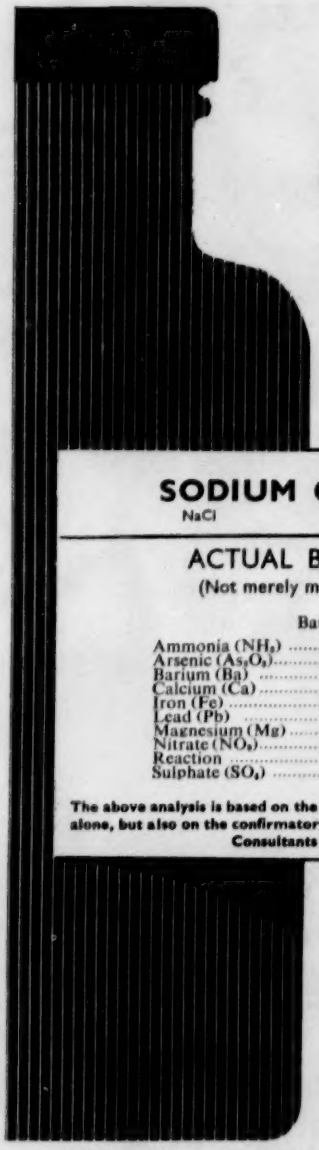

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Barium (Ba)	no reaction
Calcium (Ca)	0·0012%
Iron (Fe)	0·00004%
Lead (Pb)	no reaction
Magnesium (Mg)	no reaction
Nitrate (NO_3)	0·0006%
Reaction	pH 7·05
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The Kinetics of the Reduction of Azoxybenzene (and Some Derivatives) by Titanous Chloride.

By M. J. Stephen and Sir Cyril Hinshelwood.

[Reprint Order No. 5959.]

It is concluded that the reduction of azoxybenzene by titanous chloride in aqueous alcohol proceeds as follows: (*a*) azoxybenzene ⟶ aniline; (*b*) azoxybenzene ⟶ azobenzene ⟶ hydrazobenzene ⟶ benzidine + aniline. About 20% of the total follows (*a*) which is believed to depend upon dissociation of the binuclear compound after a first (rate-determining) stage of reduction. In (*b*) the velocity constants of the first and the second stage are of comparable magnitude, and the azobenzene concentration passes through a maximum.

The initial rate of reduction of the azoxybenzene is proportional to $[TiCl_3]$, and to [Ph·NO:NPh], and the whole system is an example of second-order consecutive reactions, the kinetics of which have been worked out. The initial rate is approximately proportional to $1/[H^+]$.

The influence of substituent groups on the rate is in the few examples tested considerably smaller than in the reduction of substituted nitrobenzenes.

There are large differences (which are discussed) in the effects of acid concentration on the titanous chloride reduction of nitrobenzene, azoxybenzene, and azobenzene.

The present study of the reduction by titanous chloride of azoxybenzene and some derivatives continues previous work on the reaction of nitrobenzene and azobenzene and their derivatives (Newton, Stubbs, and Hinshelwood, *J.*, 1953, **3384**; Large, Stubbs, and Hinshelwood, *J.*, 1954, **5211**). It proves less suitable for the investigation of energy–entropy relations and of additive effects in series of substituted compounds, the influence of the substituent groups being rather small. The reaction of titanous chloride with the azoxy-compound presents, however, certain interesting contrasts with that with the nitro- and azo-compounds, and incidentally furnishes a good example of second-order consecutive reactions.

Experimental

The following reagents were used: titanous chloride, a solution in hydrochloric acid standardised with "AnalaR" ferric ammonium sulphate; azoxybenzene, recrystallised from alcohol, m. p. 35—36°; *pp'*-azoxyanisole, prepared according to Vorländer (*Ber.*, 1907, **40**, 1423), m. p. 116°; *mm'*-azoxyanisole, prepared according to Rotarski (*Ber.*, 1908, **41**, 865), m. p. 50°; *mm'*-azoxyaniline, prepared according to Andrews (*J.*, 1896, **69**, 8), m. p. 146—148°; *pp'*-azoxyaniline, prepared according to Mixter (*J. Amer. Chem. Soc.*, 1883, **5**, 2), m. p. 184°.

The method of studying the rate of reduction of the azoxy-compounds by titanous chloride consisted in the addition of samples of the reaction mixture to excess of ferric alum and back-titration with titanous chloride, the disappearance of the red colour from 0·5 ml. of 10% aqueous ammonium thiocyanate indicating the end-point. It was found convenient to have two titanous chloride solutions, one exactly 0·2M and the other exactly 0·05M, the first for making up the reaction mixtures and the second for the titrations. The hydrochloric acid concentration of both solutions was adjusted and controlled by titration with standard sodium hydroxide in conjunction with a pH-meter, the titanous hydroxide precipitate making acid–base indicators useless. The titanous chloride solutions were stored in reservoir burette systems in an atmosphere of hydrogen. The reaction mixture itself was made from equal volumes of alcohol and aqueous hydrochloric acid, titanous chloride in hydrochloric acid being mixed with the azoxy-compound in alcohol at zero time, in an Erlenmeyer flask placed in a thermostat. A non-oxidising atmosphere above the mixture was maintained by a stream of carbon dioxide saturated with alcohol. At the time of mixing both reagents were at the temperature of the

bath. The titanous chloride was added by a pipette, so calibrated that the volume introduced would be 50 ml. at 18°.

At intervals of time, samples (normally 10 ml.) of the reaction mixture were pipetted into a measured excess of ferric alum, each pipette being first well flushed with carbon dioxide. The residual ferric alum was back-titrated with titanous chloride as in the standardisation. Two corrections had to be applied, one for the contraction in volume on mixture of alcohol and water, the second for thermal expansion at the higher temperature. The total correction varied between 1·5 and 3%, the calculated values being verified by tests with solutions of titanous chloride and alcohol.

From such measurements curves were plotted showing percentage reaction against time. The initial rate obtained from the tangent to the curve at zero time can be expressed in moles of $TiCl_3$ $l.^{-1}$ $sec.^{-1}$ and if the reaction is of the second order can be written in the form :

$$\text{initial rate (above units)} = k_0[TiCl_3][\text{azoxybenzene}]$$

where k_0 is the specific rate constant and the reactant concentrations expressed in moles $l.^{-1}$ are those initially present. When the initial rate is required in terms of moles of azoxybenzene $l.^{-1}$ $sec.^{-1}$, the appropriate stoicheiometric factor must be introduced, and k_0 is replaced by another constant.

From experiments with an excess of titanous chloride left until all the azoxybenzene had been reduced, it was found that 1 mole of azoxybenzene is equivalent to 4·65 moles of titanous chloride, and not to 6 moles as would have been expected if azoxybenzene were reduced completely to aniline. These " infinity " runs were carried out in flasks having greased ground-glass stoppers and first well flushed out with carbon dioxide. This procedure was necessary because even a gentle current of carbon dioxide caused appreciable evaporation over a long period of time. These tests usually lasted at least two days, after which carbon dioxide was again passed, and samples were run into an excess of ferric alum and back-titrated as usual. Blank tests were also made with titanous chloride alone.

Azoxybenzene was found to yield partly benzidine and partly aniline. The benzidine produced was estimated as follows. The solution, after the axoxybenzene had been completely reduced, was made alkaline with sodium hydroxide and then extracted with ether which removed the aniline and benzidine. The ether was extracted with 0·25N-hydrochloric acid and to the extract 2 ml. of M-sulphuric acid were then added. The solution was left in ice water for 30 min. to ensure the complete precipitation of benzidine sulphate, which was filtered off at the pump and well washed with ice-cold water saturated with benzidine sulphate, and finally with a little cold aqueous alcohol. The precipitate was transferred to a flask and titrated with standard sodium hydroxide. Towards the end of the titration the solution was boiled. This method was tested on a standard benzidine solution and shown to be satisfactory. It was found that 67·5% of the azoxybenzene is reduced to benzidine. Moderate changes in concentration of titanous chloride or hydrochloric acid do not appreciably affect the degree of conversion.

In an attempt to identify intermediate products in the reaction, absorption spectra of samples at different times were determined, and compared with those of azoxy- and azobenzene. Azobenzene was thus shown to be an intermediate. The amount was determined at a series of times from the absorption of samples at 430 and 450 μ, where the absorption due to azoxybenzene, aniline, and benzidine is negligible. A calibration curve under the conditions prevailing was constructed by use of a standard solution of azobenzene.

The second phase of the investigation involved the determination of activation energies for azoxybenzene and substituted derivatives, with some of which the sparing solubility necessitated lower working concentrations. The titanous equivalent of each azoxy-compound had to be determined, as the presence of substituents affected the final benzidine : aniline ratio. The temperature range extended from 10° to 40°, and at least 5 temperatures were used for activation-energy determination. The thermostats operating between room temperature and 40° were electrically heated water-baths. That for work below room temperature was an insulated methyl alcohol–water bath with a set of internal coils through which a cooling liquid was pumped from a refrigerator.

The energies of activation were determined by plotting the logarithm of the time for 10% reaction, 20% reaction, and so on against the reciprocal of the absolute temperature and finding the slope of each line by the method of least squares. The calculated values of E for various percentage reactions could if necessary be extrapolated to zero reaction to give the initial activation energy.

Results

Products of Reduction.—The amounts of titanous chloride consumed at the end of the reaction are shown in Table 1. The mean titanous chloride equivalent of azoxybenzene is 4·65 moles.

Table 1. *Stoicheiometric ratios.*

Initial [azoxybenzene], $42{\cdot}7 \times 10^{-4}$ mole $l.^{-1}$; oxidation time, 3 days.

Initial $[TiCl_3]$ (10^{-4} mole $l.^{-1}$)	515	515	643	643
Final $[TiCl_3]$ (10^{-4} mole $l.^{-1}$)	315	317	445	448
$TiCl_3$/azoxybenzene (moles)	4·69	4·65	4·65	4·59

There are two products of reduction, aniline and benzidine. Estimation of the benzidine produced showed that 67·5% of the azoxybenzene is reduced to benzidine. This is consistent with the figure of 4·65 for the titanous equivalent.

Order of Reaction.—Reaction–time curves for the reduction of azoxybenzene by titanous chloride at 25° were plotted to determine the dependence of the rate on the initial concentrations of azoxybenzene, titanous chloride, and acid severally. The initial rates of reaction expressed as moles of titanous chloride $l.^{-1}$ $min.^{-1}$ were read off from the curves. A linear relation was found when the initial rate was plotted against the initial concentration of azoxybenzene or of titanous chloride, indicating the first order of reaction with respect to each. These results are shown in Tables 2 and 3. A linear relation was also found when the initial rate was plotted against the reciprocal of the acid concentration. The line did not, however, pass through the origin and the rate was found to be expressed closely by the equation $[H^+](\text{Rate} - 0{\cdot}6) = \text{const.}$ (Table 4).

Table 2. *Variation in concentration of azoxybenzene.*

25°; $[TiCl_3] = 515 \times 10^{-4}$ mole $l.^{-1}$; $[HCl] = 515 \times 10^{-3}$ mole $l.^{-1}$.

Initial rate (10^{-4} mole of $TiCl_3$ $l.^{-1}$ $min.^{-1}$)	22·8	20·0	16·9	14·3	8·6	5·9
Initial [azoxybenzene] (10^{-4} mole $l.^{-1}$)	137·6	120·0	103·0	86·0	51·6	34·4
Rate/concn.	0·166	0·167	0·164	0·166	0·167	0·171

(Note: The drawing of tangents to curves is inevitably somewhat arbitrary, but for any given series a consistent convention was adopted so that the relative values are considered reliable, though they may differ from the true absolute values.)

Table 3. *Variation in concentration of titanous chloride.*

25°; [Azoxybenzene] = 86 × 10^{-4} mole $l.^{-1}$; [HCl] = 515 × 10^{-3} mole $l.^{-1}$.

Initial rate (10^{-4} mole of $TiCl_3$ $l.^{-1}$ $min.^{-1}$)	19·8	16·5	14·0	9·5	7·0	4·5
Initial $[TiCl_3]$ (10^{-4} mole $l.^{-1}$)	825	722	618	412	309	206
Rate/concn.	0·0240	0·0228	0·0227	0·0231	0·0227	0·0218

Table 4. *Variation in concentration of acid.*

25°; [Azoxybenzene] = 110 × 10^{-4} mole $l.^{-1}$; $[TiCl_3] = 515 \times 10^{-4}$ mole $l.^{-1}$.

Initial rate (10^{-4} mole of $TiCl_3$ $l.^{-1}$ $min.^{-1}$)	29·0	19·0	10·5	8·0	6·0	4·5	3·5
[HCl] (mole $l.^{-1}$)	0·258	0·368	0·703	0·906	1·33	1·75	2·31
10^4 [HCl] (Rate − 0·6)	7·33	6·77	6·96	6·72	7·18	6·82	6·69

A closer study of the entire titanous chloride–azoxybenzene reaction–time curve showed, however, that a second-order equation was not satisfactorily followed (Table 5). k_0 is

Table 5. *Variation of velocity constant.*

25°; Initial [azoxybenzene] = 110 × 10^{-4} $mole^{-1}$.
Initial $[TiCl_3] = 515 \times 10^{-4}$ mole $l.^{-1}$.

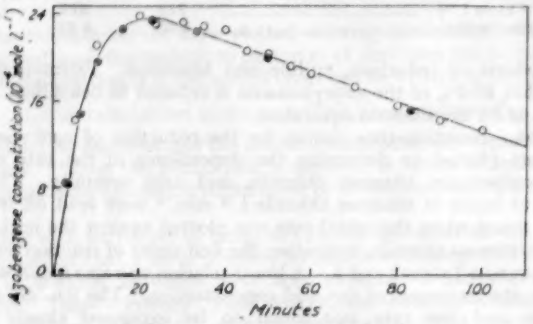
Reaction (%)	5	10	15	20	25	30	35	40	45
Time (min.)	1·6	4·0	7·1	10·8	15·1	20·0	25·2	31·8	40·6
k_0 {$sec.^{-1}$ l. (mole of $TiCl_3)^{-1}$} × 10^2	1·07	0·90	0·80	0·75	0·72	0·70	0·70	0·68	0·65

calculated from the expression: $k_0 = x/at(a - x)$ where a is initial concentration of reactants (stoicheiometrically equivalent) expressed, as moles of $TiCl_3$ $l.^{-1}$, and x is the amount which reacted in time t.

To account for the decrease in k_0, intermediate products in the reaction were looked for. The absorption spectra of samples after different times of reaction were compared with those of

azo- and azoxy-benzene, and azobenzene was found to be an intermediate. A curve showing the amount of azobenzene present at various times during the reaction is shown in Fig. 1. The form of this curve together with that for the variation in initial reactants is dealt with theoretically in the Discussion section, but it should be mentioned here that k_0 of Table 5 is only a conventional value since in the full treatment special conversions by the appropriate stoicheiometric factors are necessary.

FIG. 1. *Formation of azobenzene during reduction of azoxybenzene.*



○, Experimental; ⊗, calculated.

The effect, on the rate, of chloride ions (in the form of sodium chloride added initially to the reaction mixture) is shown in Table 6.

TABLE 6. *Effect of sodium chloride.*

[Azoxybenzene] = 110 × 10^{-4} mole $l.^{-1}$; [$TiCl_3$] = 515 × 10^{-4} mole $l.^{-1}$; [HCl] = 515 × 10^{-3} mole $l.^{-1}$.

[NaCl] (mole $l.^{-1}$)	0	0·223	0·333	0·444	0·555
Initial rate (mole of $TiCl_3$ $l.^{-1}$ $min.^{-1}$)	18·0	18·0	18·4	18·6	18·9

Activation Energy.—For the reduction of azoxybenzene, reaction–time curves between 10° and 40° and for acid concentrations of 0·256, 0·515, and 2·84N were determined. From these curves Table 7 was prepared.

TABLE 7. *Temperature coefficients for azoxybenzene.*

	Time (min.) for given % reaction at							Activation energy (kcal./mole)
	10°	15°	20°	25°	30°	35°	40°	
[HCl] = 0·256N; [Azoxybenzene] = 110 × 10^{-4} mole $l.^{-1}$; [$TiCl_3$] = 515 × 10^{-4} mole $l.^{-1}$.								
10%	6·6	4·3	2·7	1·9	1·3	—	—	16·8
20%	18·2	12·1	6·1	4·2	2·8	—	—	16·6
30%	27·7	17·1	11·0	7·1	4·8	—	—	17·3
40%	—	33·2	18·6	11·7	7·7	—	—	17·0
								Mean 16·9
[HCl] = 0·515N; [Azoxybenzene] and [$TiCl_3$] as above.								
10%	—	13·0	8·3	4·8	3·2	2·1	1·4	15·8
20%	—	31·0	17·7	10·2	7·0	4·5	3·0	16·3
30%	—	—	33·5	19·1	12·0	7·5	5·1	16·5
40%	—	—	—	28·8	17·8	11·1	7·6	17·2
								Mean 16·4
[HCl] = 2·84N; [Azoxybenzene] and [$TiCl_3$] as above.								
10%	—	—	30·2	19·3	12·0	7·7	5·0	16·3
20%	—	—	64·6	41·2	25·7	16·2	10·6	15·9
30%	—	—	107	67·8	42·5	27·5	17·1	16·5
								Mean 16·2

General mean E = 16·5 kcal./mole.

For the substituted azoxybenzenes similar results are given in Table 8.

TABLE 8. *Temperature coefficients for substituted azoxybenzenes.*

	Time (min.) for given % reaction at					Activation energy (kcal./mole)
	20°	25°	30°	35°	40°	
			pp'-Azoxyanisole.			
10%	63	43	33	21	13·5	15·0
20%	151	110	74	48	35	14·7
						Mean 14·8
			mm'-Azoxyanisole.			
10%	3·5	2·7	1·6	1·2	0·8	13·3
20%	11·0	7·9	5·1	3·8	2·1	14·1
30%	24·5	17·4	10·1	7·6	5·0	14·0
						Mean 13·8
			pp'-Azoxyaniline.			
10%	5·0	4·0	3·3	2·7	2·3	15·2
20%	10·4	8·5	6·9	5·7	4·7	15·2
30%	16·8	13·7	11·3	9·2	7·6	15·2
						Mean 15·2
			mm'-Azoxyaniline.			
10%	4·0	2·5	1·6	1·0	0·7	15·3
20%	10·0	5·9	3·9	2·6	1·7	15·2
30%	—	14·5	8·4	6·2	3·9	15·4
						Mean 15·3

DISCUSSION

Kinetics.—The reduction of azoxybenzene to benzidine and aniline by titanous chloride in acid solution takes place according to the equations :

$$Ph{\cdot}NO{:}N{\cdot}Ph + 4H \longrightarrow NH_2{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}NH_2 \quad . \quad . \quad . \quad . \quad . \quad 68\%$$
$$Ph{\cdot}NO{:}N{\cdot}Ph + 6H \longrightarrow 2Ph{\cdot}NH_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad 32\%$$

Large, Stubbs, and Hinshelwood (*J.*, 1954, 2736) showed that azobenzene in acid solution is reduced as follows by titanous chloride

$$Ph{\cdot}N{:}N{\cdot}Ph + 2H \longrightarrow NH_2{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}NH_2 \quad . \quad . \quad . \quad . \quad . \quad 84\%$$
$$Ph{\cdot}N{:}N{\cdot}Ph + 4H \longrightarrow 2Ph{\cdot}NH_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad 16\%$$

Since only 68% of the azoxybenzene reduced is converted into benzidine compared with 84% of azobenzene it appears that approximately 20% of the azoxybenzene may be reduced directly to aniline without passing through the azobenzene stage, possibly by a dissociation of the binuclear compound after the first electron transfer on reduction. Both phenylhydroxylamine and nitrosobenzene are rapidly reduced to aniline by titanous chloride, and any intermediate stages between them will be still more unstable.

The initial reduction of azoxybenzene by titanous chloride is of the first order with respect to both azoxybenzene and titanous chloride. The reduction of azobenzene is similar in this respect. The equations for the rate of reduction may thus be formulated in the following way :

If at time t, [azoxybenzene] $= A$, [azobenzene] $= B$, [$TiCl_3$] $= T$, then

$$dA/dt = -k_1'AT - k'AT = -k_1AT \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k_1' measures the rate of reaction to azobenzene, and k' that direct to aniline.

$$dB/dt = k_1'AT - k_2BT \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

whence

$$\frac{dB}{dA} = -\frac{k_1'}{k_1} + \frac{k_2B}{k_1A}$$

Integration gives

$$B = \frac{k_1'}{k_1}\left[\frac{A_0^{1-k}A^k - A}{1-k}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $k = k_2/k_1$ and A_0 is the initial value of A. Let the amount of titanous chloride used in converting 1 mole of azoxybenzene into end products be β and that used in converting 1 mole of azoxybenzene into azobenzene be α. ($\alpha = 2$ and $\beta = 4{\cdot}7$.)

At time t the titanous chloride which has reacted is given by

$$T_0 - T = \alpha B + \beta(A_0 - A - B) \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Under conditions where stoicheiometrically equivalent proportions of azoxybenzene and titanous chloride are used, $\beta A_0 = T_0$. Substitution of (4) into (1) gives

$$-\mathrm{d}A/\mathrm{d}t = k_1 A[(\beta + l)A - lA_0^{1-k}A^k] \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

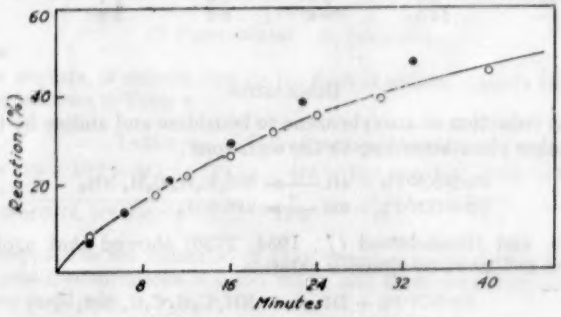
where $l = k_1'(\beta - \alpha)/k_1(k - 1)$.

Before (5) can be resolved the value of k must be known. The [azobenzene]–time curve (Fig. 1) shows a maximum, the condition for which is $\mathrm{d}B/\mathrm{d}t = 0$. Equation (2) gives at this point $k_2/k_1' = A_m/B_m$, where A_m and B_m are the values of [azoxybenzene] and [azobenzene] at the time corresponding to the maximum:

$$\beta A_m = T_m - (\beta - 2)B_m$$

Substitution of the numerical values of T_m and B_m from graphs gives $k_2/k_1' = 2{\cdot}5$.

FIG. 2. *Reaction–time curve for azoxybenzene and titanous chloride in equivalent quantities.*



○, Experimental; ⊗, calculated.

From the comparison between the amounts of benzidine formed from azobenzene and azoxybenzene respectively it has been concluded that k_1'/k_1 = fraction of reaction *via* azobenzene = 0·80.

Hence
$$k = \frac{k_2}{k_1} = \frac{k_2}{k_1'} \cdot \frac{k_1'}{k_1} = 2{\cdot}5 \times 0{\cdot}80 = 2{\cdot}0$$

Equation (5) must normally be integrated as a series which becomes indeterminate for the special value $k = 2$, but for this value it so happens that the equation becomes directly integrable and yields

$$t = \frac{1}{\rho}\left(\frac{1}{A} - \frac{1}{A_0}\right) - \frac{\varepsilon}{\rho^2} \ln \frac{A(\rho - \varepsilon A_0)}{A_0(\rho - \varepsilon A)} \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where $\rho = k_1\beta + k_1'(\beta - \alpha)$ and $\varepsilon = k_1'(\beta - \alpha)/A_0$.

If now k_1, the rate constant for azoxybenzene, is taken to be $1{\cdot}26 \times 10^{-2}$ (with time in sec. and all concentrations in mole $l.^{-1}$), k_2 is found to be $2{\cdot}52 \times 10^{-2}$ sec.$^{-1}$ l. mole^{-1}, and the curve shown in Fig. 1 for the formation of azobenzene can be calculated. It is seen to agree satisfactorily with experiment. The value of k_2 compares with the figure found by Large *et al.* of $2{\cdot}5 \times 10^{-2}$ for experiments on the direct reduction of azobenzene. From equation (6), [azoxybenzene] and [$TiCl_3$], as well as [azobenzene], were calculated as functions of time. Typical results for the consumption of titanous chloride are shown in Fig. 2.

The value $1{\cdot}26 \times 10^{-2}$ for k_1 required by Fig. 1 can be compared with a direct value

obtained approximately in a different way. From the tangent at the origin to a curve of titanous chloride consumed against time, the initial rate of disappearance of $TiCl_3$ can be found. Azobenzene is formed, and in an interval Δt after the start of the reaction has an average concentration B. The amount of titanous chloride used by the azo-compound in this interval $= M = k_2BT_0\Delta t \times 2{\cdot}32$ according to the stoicheiometric figure of Large *et al.* The total amount of titanous chloride reacting in this interval is $T_0 - T$, and of this $(T_0 - T - M)$ reacts with azoxybenzene. 80% of the azoxybenzene yields azobenzene, 20% giving aniline which requires 6 mols. of $TiCl_3$. Thus the average $TiCl_3$: azoxybenzene equivalence is $(0{\cdot}80 \times 2) + (0{\cdot}20 \times 6) = 2{\cdot}8$. Thus the amount of azoxybenzene reacting is $(T_0 - T - M)/2{\cdot}8$ and this is $k_1A_0T_0$. As $\Delta t \longrightarrow 0$, $B \longrightarrow 0$, and $k_1A_0T_0 \longrightarrow (dT/dt)_0/2{\cdot}8$. The curvature changes rather rapidly near the origin but (dT/dt) is within the range $1{\cdot}8 \times 10^{-5}$ to $2{\cdot}3 \times 10^{-5}$ where $A_0 = 110 \times 10^{-4}$ mole $l.^{-1}$ and $T_0 = 515 \times 10^{-4}$ mole $l.^{-1}$. Thus k_1 is in the range $1{\cdot}1 \times 10^{-2}$ to $1{\cdot}5 \times 10^{-2}$ which includes the value previously obtained.

From Table 4 the initial rate is seen to be nearly proportional to $1/[H^+]$. In view of the considerable hydrolysis of titanous chloride in solution it seems probable that the predominant reducing species is here $Ti(OH)^{2+}$, as was found by Yost and Zabaro (*J. Amer. Chem. Soc.*, 1926, **48**, 1181) in their study of the kinetics of the oxidation of tervalent titanium by iodine, and by Mackenzie and Tompkins (*Trans. Faraday Soc.*, 1942, **38**, 465) in a study of the autoxidation of titanous chloride. The equilibrium involved is :

$$Ti^{3+} + H_2O \rightleftharpoons Ti(OH)^{2+} + H^+$$

with

$$[Ti(OH)^{2+}] = K[Ti^{3+}]/[H^+]$$

so that the initial rate of reaction of this species with azoxybenzene may be expressed by :

$$\text{Rate} = k[\text{Azoxybenzene}][Ti(OH)^{2+}] = k_1[\text{Azoxybenzene}][Ti^{3+}]/[H^+]$$

Influence of Substituents.—Although the range of substituents investigated is not large, it seems clear that the influence is a good deal less than that observed in the reduction of nitrobenzene. Table 9 shows the rates relative to that for the unsubstituted compound for some of the derivatives in the two series.

TABLE 9. *Influence of substituents.*

Substituent	Relative rates: Nitrobenzene series	Relative rates: Azoxybenzene series
H	1	1
p(*p'*)-OMe	0·21	0·48
m(*m'*)-OMe	1·15	1·51
p(*p'*)-NH_2	2·32	1·38
m(*m'*)-NH_2	5·49	1·43

With the azoxy-compounds the range of variation is too narrow for the effective examination of energy–entropy relations, and the number of compounds examined is too small for the testing of additive relations in the free energies of activation. Nevertheless the relative insensitiveness to the effect of the substituent is itself of interest, and may be connected with the influence of hydrion concentration just referred to. With nitrobenzene the reduction rate is proportional nearly to $1/[H^+]^2$ and with azoxybenzene to $1/[H^+]$. Thus, if it is assumed (which of course is not absolutely necessary) that the reducing species is the same in each case, then in the expression for the reaction rate of the azoxy-compound an extra term $[H^+]$ occurs. This might indicate that an extra proton must be present in the transition state. If so, the attachment of this proton would be antagonised by a recession of electrons from the reaction centre, an effect which would tend to neutralise the correspondingly easier transfer of electrons from the reducing agent. Such compensating influences may explain the small total change in rate caused by the substituent groups.

It is also of interest to note that, for comparable conditions of acidity, the azoxy-compounds have lower activation energies than the corresponding nitro-compounds

although they are usually reduced more slowly. The entropy of activation is lower. This may be because the transfer of electrons from the titanium to the reaction centre is easier, but that the presence of suitably placed protons to provide the hydrogen for reduction has, with the binuclear compound, become a more critical need. In the discussion of azobenzene reduction it has already been tentatively suggested that the appropriate proton supply is a very important factor. Such a conclusion rests upon the observation that the rate of reaction depends in a quite remarkable way on the acidity. The activation energy, on the other hand, is even lower than for the azoxy-compounds. The following numbers illustrate these relations ($k = Ae^{-E/RT}$).

	E	$\log_{10} A$ for reaction in 0·5N-acid
Nitrobenzene	17,700	12·9
Azoxybenzene	16,500	10·2
Azobenzene	15,800	10·1
p-Aminonitrobenzene	16,500	11·6
pp'-Diaminoazoxybenzene	15,200	9·5
p-Aminoazobenzene	12,700	8·4

Note on Reduction of Nitrobenzene.—The fact that the reduction of azoxybenzene by titanous chloride yields a considerable proportion of benzidine re-opens a question about the course of reduction of nitrobenzene. Newton, Stubbs, and Hinshelwood (*J.*, 1953, 3384) found that the second-order rate constants for this reduction fell as the reaction proceeded, and attributed the fall to the known possibility of interaction between the intermediates nitrosobenzene and phenylhydroxylamine to give azoxybenzene, which they showed in fact to be reduced at about the rate required to account for the later part of the nitrobenzene reduction. No further consequences depended upon this assumption since the definitive results were expressed in terms of initial rates of reaction. It needs some revision, however, since nitrobenzene yields aniline quantitatively, and, at any rate with a moderate excess of titanous chloride present, no benzidine at all is found. Fresh experiments to elucidate this point have shown :

(*a*) that under actual conditions of the reaction the condensation of nitrosobenzene and phenylhydroxylamine is not rapid enough to divert a serious amount of the nitrobenzene through the azoxybenzene route (the curves of titanous chloride consumption which seemed in the previous work to indicate the contrary can be explained by the fact that phenylhydroxylamine is easily re-oxidised by ferric alum) ;

(*b*) that phenylhydroxylamine and titanous chloride give a reaction which remains of the second order over most of its course (the corresponding reduction of nitrosobenzene being too fast to measure) ; and

(*c*) that over the greater part of the reaction course nitrobenzene (determined by extraction and photometry) and titanous chloride are removed from the system in very nearly the stoicheiometric ratio corresponding to aniline formation.

The fall in the second-order constants with time in the course of the nitrobenzene reduction is now attributed to a combination of several factors, including, first, the not strictly linear proportionality of the active titanous species to the total concentration, and, secondly, small diversion of the reaction through more difficultly reduced intermediate products, or formation of aminophenol towards the end of the reduction (though this does not occur when the titanous chloride is in excess and is in any case less than was supposed). Although the reaction products added to a fresh reacting mixture have been shown to have no retarding effect, it remains a possibility that they cause slow changes in the state of co-ordination of the reducing titanous species and so impair its activity in some degree.

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Isotopic Exchange of Copper between Cupric Nitrate and the Metal.

By J. F. Duncan and B. W. Oakley.

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The isotopic exchange of copper between cupric nitrate and powdered metal has been studied. Although rapid apparent exchange reactions are observed it is shown that they are critically dependent on the nature of the surface, and are in particular enhanced in oxidising environments. By carefully preparing a fresh unoxidised copper surface by electrolysis it is shown that the true exchange reaction between the clean metal surface and the solution is not complete even after 14 hours.

Isotopic exchange reactions between metals and aqueous solutions of their salts have been studied by a number of previous workers (Haissinsky, *J. Chim. phys.*, 1948, **45**, 224; 1949, **46**, 298; Haissinsky and Cottin, *ibid.*, p. 476; Baerg and Winkler, *Canad. J. Chem.*, 1953, **31**, 319, 521; Rollin, *J. Amer. Chem. Soc.*, 1940, **62**, 86). In almost all cases they report a rapid initial reaction for a few minutes, followed by a slow loss of activity from solution during many hours or days. Baerg and Winkler (*loc. cit.*) suggested that the kinetics of the silver ion–metal exchange reaction indicate the occurrence of several different exchange reactions on the surface of the same specimen of metal, which was interpreted as due to the presence of crystal faces of different orientation. We obtain similar results to theirs with the analogous copper system, but our results show that the exchange reaction between metallic copper and cupric nitrate is very slow. In this case the apparent rapid exchange reaction is due to secondary surface reactions, probably with an oxide film.

Experimental and Results

50 ml. of a solution of cupric nitrate, of appropriate concentration and pH (adjusted by addition of a little ammonia solution), were stirred vigorously, the speed of the stirrer being recorded. Radioactive ^{64}Cu (half-life 12·88 hr.) as nitrate, obtained by pile irradiation of cupric nitrate, was added to give an activity of about 8000 counts/min./ml. About 0·5 g. of electrolytic copper powder (~200 mesh) was next added. At varying intervals afterwards, 0·5 ml. of solution was removed through a sintered-glass filter attached to the bottom of the pipette. This was placed in a small beaker and presented in a reproducible position to the window of a Geiger–Müller counter, and the activity determined with the usual corrections for circuit paralysis time, background, decay, etc.

Results.—In most cases, any loss of activity from solution occurred within 10 min., the solution remaining unchanged thereafter. To elucidate the nature of the reaction occurring, the effect of the following variables was studied.

(a) *Stirring rate.* The total percentage drop in activity obtained when the solution activity had become constant was dependent on the rate at which the cupric nitrate was agitated (see Fig. 1). At high stirring rates considerable scatter of the results was obtained owing to the presence of variable amounts of air bubbles.

(b) *Environment.* The percentage uptake of activity was redetermined when using (i) oxygen and (ii) nitrogen from cylinders at constant stirring rate, with a gas flow as great as could be allowed without causing loss of liquid. Table 1 shows that oxygen causes con-

Table 1. *Observed percentage change in activity under different conditions.*

(Solution stirred at 450 rev./min.; pH = 2.)

Condition of experiment	Wt. of Cu, g.	Loss (%) of activity from solution
(1) Normal stirring in air	0·494	2·3
(2) Air blown through solution	0·495	3·2
(3) Oxygen blown through solution	0·493	6·5
(4) Nitrogen blown through solution	(*a*) 0·483, (*b*) 0·494	(*a*) 1·1, (*b*) 0·1

siderable enhancement of the initial reaction. This suggests that the initial reaction is associated with the surface oxidation of the copper.

(c) pH *Dependence.* To satisfy ourselves that these effects were not associated with other changes in environment, the reaction was followed at constant stirring rate in solutions of different pH and different cupric-ion concentrations. The magnitude of the initial loss of activity from solution was found to be constant for $0{\cdot}8 < \text{pH} < 3{\cdot}6$, falling to zero at pH ~0 (see Fig. 2). This is in accordance with the suggestion that the activity loss is due to the presence of a surface-oxidised copper, since at high acidity, surface oxidation would be small.

FIG. 1. *Variation of percentage drop in activity with stirring rate.*

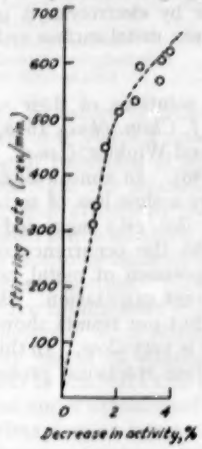


FIG. 2. *Effect of* pH. (0·496 ± 0·001 *g. copper. Stirring rate* 540 *revs./min.* N-*copper nitrate.*)

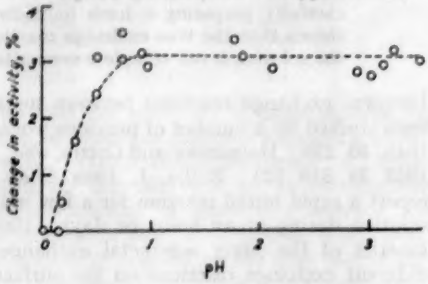


FIG. 3. *Effect of copper nitrate concentration.* (0·499 ± 0·001 *g. copper. Stirring rate* 540 *revs./min.* pH = 2·00.)

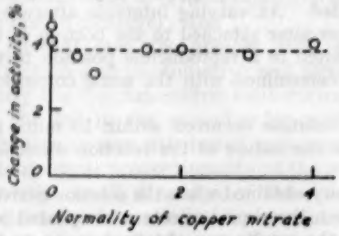
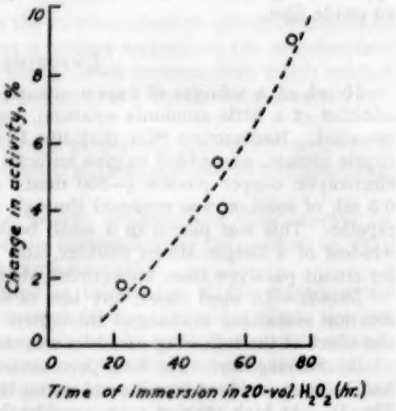


FIG. 4. *Effect of immersion of copper in* 20-*vol. hydrogen peroxide, prior to reaction with active cupric nitrate.*



(d) *Concentration.* At a pH of 2 and with a stirring rate of 540 rev./min., the concentration was varied over the range 0·001—4N-cupric nitrate (see Fig. 3). The percentage activity drop was independent of concentration. Hence the magnitude of the apparent exchange reaction is proportional to the concentration. This would not be expected if the reaction were a simple surface exchange but it would occur if the reaction took place in either a chemically formed or an adsorbed surface layer the amount of which was proportional to the cupric-ion concentration.

(e) *State of copper surface.* If the copper powder (inactive) is added to inactive cupric nitrate, and after 15 min. or more the solution is seeded with active copper nitrate, no loss in activity from the solution occurs, except when the solution is thoroughly saturated with oxygen by bubbling (see Table 2). A similar result is obtained with copper powder which has been previously etched in acid.

TABLE 2. *Pretreatment of copper.*

(pH = 2; 540 rev./min.; N-cupric nitrate; 0·497 ± 0·002 g. of copper.)

Pre-treatment	Change in activity, %
(1) None	2·3
(2) Cu left for 1 hr. in N-$Cu(NO_3)_2$	0·0
(3) As (2), oxygen blown into reacting solution	2·4
(4) Etched for ½ min. in 8N-HNO_3; dried on filter-paper before use in exchange reaction	0·2

By setting the copper aside for varying periods in solutions of 20-vol. hydrogen peroxide, it was found that the activity loss from solution in a subsequent exchange experiment was dependent on the length of time the copper had been in the peroxide solution; in many cases it was very large (see Fig. 4).

Since it is now clear that the rapid uptake of activity obtained in most cases is due to a secondary surface reaction, it follows that a careful preparation of the surface of the copper is necessary if we are to be sure that we are measuring the true exchange reaction between copper metal and cupric ions. For this purpose an electrolytic method of preparation is probably most satisfactory.

A flat piece of copper wire gauze (~150 mesh) was made one electrode in a conventional electrolytic apparatus for the analysis of copper in solution. The other electrode was a cylindrical piece of platinum gauze inside which the copper gauze rotated. The solution (N/100-copper nitrate) was electrolysed for 2 hr. Electrolysis was stopped, but stirring was continued, and the copper activity was then introduced into the system. Aliquot portions of the solution were removed at different times and the activity was measured. The results are quoted in Table 3.

TABLE 3. *Observed initial drop in activity after electrolysis.*

State of copper gauze before experiment	Change in activity initially, %	State of copper gauze before experiment	Change in activity initially, %
Cathode	(*a*) 0·0, (*b*) 0·1	Anode	(*a*) 4·35, (*b*) 4·25

There was a significant change in activity obtained when the copper gauze had been used as the anode. Anode electrolysis would probably lead to some surface oxidation and presumably this accounts for the observed change. No change in activity was initially detectable after the copper had been used as cathode, although there was a slow loss extending over many hours. This was, however, only about ½% per hr., but was continuous for at least 14 hr. It was calculated that, if complete exchange with a monolayer on the surface took place, a change of about ½% in the activity would occur if the superficial area of the wire could be taken as equal to its real area. As the real surface is probably an order of magnitude greater than the apparent surface, it is clear that any exchange reaction which is occurring is very slow. We conclude therefore that, unless copper is unique in this respect, the rate of isotopic exchange between a clean metal surface and an aqueous solution of its ions is much slower than is commonly believed.

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Organic Oxidation Processes. Part III. The Reaction of Lead Tetra-acetate with Some Phenyl Ethers.*

By G. W. K. Cavill and D. H. Solomon.

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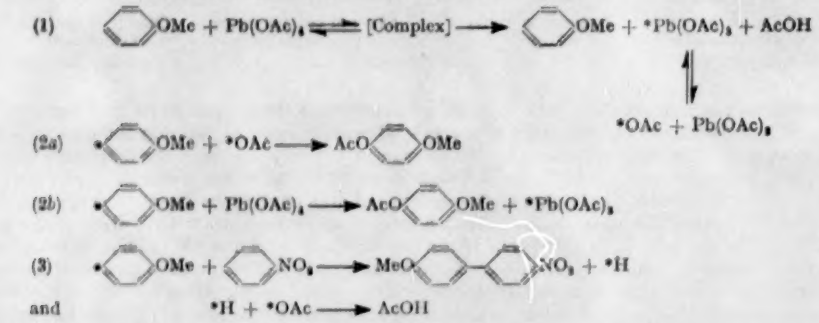
The *p*-acetoxylation of anisole and of related phenyl ethers by lead tetra-acetate is described. The mechanism of the reaction is discussed, especially with reference to solvent effects.

Alkylphenols are readily oxidised by lead tetra-acetate in acetic acid or benzene at room temperature (Part I, *J.*, 1954, 2785), but phenol derivatives such as anisole or benzyl phenyl ether not at all. At 80°, benzyl phenyl ether yields *p*-acetoxyphenyl benzyl ether together with the expected product of oxidation at the α-methylene group (Barron, Cavill, Cole, Gilham, and Solomon, *Chem. and Ind.*, 1954, 76).

The *p*-acetoxylation of phenyl ethers, and related reactions, are now reported in detail. Anisole, phenetole, and phenyl *iso*propyl ether with lead tetra-acetate in acetic acid at 80° give the *p*-acetoxy-ethers: the yields are small, unchanged ether is recovered, and no attack on the alkyl group is observed. Anisole yields as additional products 4-methoxydiphenyl in benzene, 4-methoxy-4′-nitrodiphenyl in nitrobenzene, and 4 : 4′-dimethoxydiphenyl in excess of anisole, which, since they result from an attack on the solvent, indicate a free-radical mechanism.

We suggest a primary dehydrogenation by lead tetra-acetate to give *p*-methoxyphenyl and acetate radicals with acetic acid and lead acetate. Subsequent reactions are as in (2*a* and *b*). Kharasch, Friedlander, and Urry (*J. Org. Chem.*, 1951, **16**, 533) proposed a



similar mechanism for the initial breakdown of lead tetra-acetate in di*iso*propyl ether. Reaction with the solvent is exemplified for nitrobenzene in (3); other isomers may have been formed but were not identified. The 4 : 4′-dimethoxydiphenyl formed in absence of added solvent may result from attack on anisole by the *p*-methoxyphenyl radical (3) or from dimerisation of the radical.

No chlorinated anisole derivative was detected on oxidation in carbon tetrachloride, which gave *p*-acetoxyanisole and *p*-methoxyphenyl *p*-anisoate. That no attack on the solvent occurs indicates that the *p*-methoxyphenyl is less reactive than the phenyl radical [cf. Kharasch, Kane, and Brown's observations (*J. Amer. Chem. Soc.*, 1942, **64**, 1621) on the relative reactivity of free radicals]. The formation of the *p*-anisoate, although indicative of the *p*-methoxyphenyl radical in solution, is unexpected and the mechanism is not yet understood.

Wessely, Kotlan, and Metlisics (*Monatsh.*, 1954, **85**, 69) showed that methyl α-naphthyl ether is oxidised to the 4-acetoxy-1-naphthyl methyl ether with lead tetra-acetate in acetic acid at room temperature, and suggest that primary attack of an acetate radical (from

* Part II, *J.*, 1954, 3943.

lead tetra-acetate at room temperature) yields the 4-methoxy-1-naphthyl radical and acetic acid; 4-acetoxy-1-naphthyl methyl ether then results from a combination of the naphthyl and acetate radicals. 4 : 4'-Dimethoxydi-1-naphthyl was also isolated. As we have treated anisole with acetyl peroxide in acetic acid–ether to 80° without apparent oxidation we believe that the acetate radical is not responsible for the primary dehydrogenation of phenyl ethers.

As noted in our preliminary communication (*loc. cit.*, p. 76) two competitive reactions occur with benzyl phenyl ether, *viz.*, *p*-acetoxylation and attack at the α-methylene group. The nuclear substitution is analogous to that in anisole. Attack at the α-methylene group yields α-phenoxybenzyl acetate, identified by hydrolysis in alkali to benzaldehyde and phenol. The yield in this reaction is small compared with that of benzyl acetate from toluene (cf. Part II, *loc. cit.*), and it is of further significance that benzyl *p*-tolyl ether is oxidised to *p*-benzyloxybenzyl acetate (isolated as the alcohol) in high yield, no attack at the α-methylene group being observed.

In conclusion we emphasise that the primary process in the oxidation of phenyl ethers is an attack by the lead tetra-acetate which results in the dehydrogenation of the substrate. The final products isolated are determined by interactions of the intermediate radicals and/or by their reaction with oxidant, substrate, and solvent.

The acetoxylation of phenyl ethers contrasts with Fieser, Clapp, and Daudt's methylations of benzenoid compounds (*J. Amer. Chem. Soc.*, 1942, **64**, 2052). They reported that benzene was converted into benzyl acetate, nitrobenzene into *o*- and *p*-nitrotoluene, and chlorobenzene into a mixture of chlorobenzyl acetates, the *para*-isomer being identified. [Their isolation of nitrotoluenes and not nitrobenzyl acetates is explicable, for the nitro-group strongly deactivates the toluene towards further oxidation (cf. Part II, *loc. cit.*).] Thus nuclear acetoxylation by lead tetra-acetate occurs in benzenoid compounds containing a powerful electron-donating substituent but methylation, by methyl radicals from decomposition of lead tetra-acetate, is favoured in compounds having electron-attracting substituents. Acetoxylation of the side-chain may be the preferred reaction of lead tetra-acetate with an alkylbenzene.

Experimental

Oxidation of Anisole with Lead Tetra-acetate.—(*a*) Anisole (32·4 g.; freshly distilled over sodium) with lead tetra-acetate (133 g.) in " AnalaR " acetic acid (120 ml.) was heated at 80° (oil-bath) until no positive test (starch–iodide) for the oxidant was obtained (40 hr.). Acetic acid was distilled off under reduced pressure, and the residue was then extracted with ether (6 × 50 ml.), lead acetate remaining. The ethereal solution, washed with water, sodium hydrogen carbonate solution, water, and then dried ($MgSO_4$) and evaporated, gave a viscous yellow oil, which, under reduced pressure, yielded unchanged anisole, n_D^{20} 1·5171, and *p*-acetoxyanisole (7·0 g., crude), b. p. 96°/3 mm., colourless needles, m. p. 32°, from light petroleum (b. p. 40—60°) (Found: C, 65·4; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·1%). Klemenc (*Monatsh.*, 1914, **35**, 85) records m. p. 31—32°. No formaldehyde was detected.

(*b*) Anisole (7·0 g.) with lead tetra-acetate (28·8 g.) in acetic acid (40 ml.) was heated at 80° (111 hr.). The mixture, hydrolysed with excess of aqueous sodium hydroxide, was then steam-distilled to yield anisole (5·0 g., n_D^{20} 1·5180), recovered by extraction with ether. Similar extraction of the residual solution, after acidification, gave *p*-hydroxyanisole (1·2 g.), obtained as colourless needles, m. p. and mixed m. p. 50—51°, from water.

(*c*) Anisole (32·4 g.) with lead tetra-acetate (133 g.) in benzene (120 ml.; freshly distilled over sodium) was heated at 80° (90 hr.). The mixture, worked up as in (*a*), gave unchanged anisole, n_D^{20} 1·5176, *p*-acetoxyanisole (3·0 g., crude), and a semisolid residue (0·5 g.). On redistillation, the *p*-acetoxyanisole was obtained as an almost colourless oil, b. p. 94°/3 mm. (Found: C, 65·2; H, 6·2%). The semisolid residue, after chromatography on alumina from light petroleum, yielded 4-methoxydiphenyl (0·1 g.), colourless needles, m. p. 88—89° (from aqueous ethanol) (Found: C, 84·4; H, 6·6. Calc. for $C_{13}H_{12}O$: C, 84·8; H, 6·6%). Werner (*Annalen*, 1902, **322**, 135) records m. p. 90°. Further elution with benzene gave an unidentified oil (0·4 g.).

(*d*) Anisole (32·4 g.) with lead tetra-acetate (133 g.) in " AnalaR " nitrobenzene (120 ml.) was heated at 80° as above (83 hr.). The product, worked up as in (*a*), gave a mixture of anisole,

nitrobenzene, and *p*-acetoxyanisole, b. p. to 120°/1 mm., and a small residue which was chromatographed on alumina from light petroleum to yield 4-methoxy-4′-nitrodiphenyl (0·2 g.), yellow needles (from light petroleum–benzene), m. p. 109—110° (Found: C, 68·3; H, 4·95; N, 6·2. Calc. for $C_{13}H_{11}O_3N$: C, 68·1; H, 4·8; N, 6·1%). Bell and Kenyon (*J.*, 1926, 3044) record m. p. 111°. An amber-coloured oil (0·2 g.) was eluted with benzene. The presence of *p*-acetoxyanisole (2·0 g., estimated by sap. val.) was indicated by the isolation of *p*-hydroxyanisole (1·2 g.), m. p. and mixed m. p. 50—51°, on hydrolysis of the original mixture.

(*e*) Anisole (32·4 g.) with lead tetra-acetate (133 g.) in carbon tetrachloride (120 ml.; freshly distilled) was heated at 80° (100 hr.). The mixture, extracted as in (*a*), yielded anisole, *p*-acetoxyanisole (1·0 g., crude), b. p. 80—84°/1 mm., and a semisolid residue (0·5 g.). Hydrolysis of the *p*-acetoxyanisole gave *p*-hydroxyanisole (0·5 g.), m. p. and mixed m. p. 52°. The residue was chromatographed on alumina, elution with light petroleum–benzene (1 : 1) giving a compound (0·4 g.), forming colourless prisms, m. p. 123°, from ethanol [Found: C, 70·3, 69·3; H, 5·8, 5·3; Ac, 2·2%; *M* (Rast), 254. Calc. for $C_{15}H_{14}O_4$: C, 69·8; H, 5·5%, *M*, 258]; the mixed m. p. with *p*-methoxyphenyl *p*-anisoate was 123—124°.

(*f*) Anisole (150 g.) and lead tetra-acetate (133 g.) were heated at 80° for 70 hr. The mixture, after removal of excess of anisole, n_D^{20} 1·5176, gave *p*-acetoxyanisole (3·0 g., crude), b. p. 78—80°/1 mm., and 4 : 4′-dimethoxydiphenyl (2·3 g.), b. p. 134°/1 mm. A residue (0·3 g.) was not distilled. *p*-Acetoxyanisole was finally obtained as colourless needles (2·3 g.), m. p. 32°, from light petroleum (Found: C, 65·2; H, 6·1%). The 4 : 4′-dimethoxydiphenyl formed colourless needles, m. p. and mixed m. p. 174°, from alcohol after sublimation under reduced pressure (Found: C, 78·3; H, 6·8. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%).

p-*Methoxyphenyl* p-*Methoxyphenylacetate and* p-*Anisate.*—*p*-Methoxyphenylacetyl chloride (6·0 g.) (Cain, Simonsen, and Smith, *J.*, 1913, **103**, 1035) was added to sodium *p*-methoxyphenoxide [from sodium (0·8 g.) and *p*-hydroxyanisole (4·1 g.)] in toluene (20 ml.), and the mixture heated at reflux for 15 min. After working up in the usual manner, p-*methoxyphenyl* p-*methoxyphenylacetate* was obtained as colourless plates (6·5 g.), m. p. 74—74·5°, from ethanol (Found: C, 70·3; H, 5·7. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

Similarly, *p*-anisoyl chloride (5·0 g.) and sodium *p*-methoxyphenoxide gave p-*methoxyphenyl* p-*anisate* (8·0 g.), colourless prisms, m. p. 123—124°, from ethanol (Found: C, 69·5; H, 5·5. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%).

Attempted Oxidation of Anisole with Acetyl Peroxide.—Anisole (16·2 g.) in acetic acid (60 ml.) was added to acetyl peroxide (18·0 g.) (Gambarjan, *Ber.*, 1909, **42**, 4003) in ether (300 ml.). The ether was distilled off and the temperature of the mixture slowly raised to 80°. No positive test for the oxidant was obtained after 1 hr. The mixture was then hydrolysed with aqueous sodium hydroxide. Steam-distillation, followed by extraction of the distillate with ether, gave unchanged anisole (16·0 g.), b. p. 154—155°, n_D^{20} 1·5176. A sweet-smelling oil (1·0 g.), presumably resulting from oxidation of the solvent, was isolated from the acidified residue, but no phenolic products. Acetaldehyde, also from oxidation of the solvent, was isolated as the 2 : 4-dinitrophenylhydrazone (1·0 g.), m. p. and mixed m. p. 147° (Found: N, 24·9. Calc. for $C_8H_8O_4N_4$: N, 25·0%).

Oxidation of ***Phenetole and Phenyl*** iso*Propyl Ether with Lead Tetra-acetate.*—(*a*) Phenetole (36·6 g.; freshly distilled over sodium) with lead tetra-acetate (133 g.) in acetic acid (120 ml.) was heated at 80° for 40 hr. Working up as for anisole (*a*) gave unchanged phenetole, n_D^{16} 1·5080, then p-*acetoxyphenetole* (3·0 g., crude), b. p. 100°/4 mm., colourless plates (1·5 g.), m. p. and mixed m. p. 54° (from light petroleum) (Found: C, 66·5; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

p-Hydroxyphenetole (1·4 g.) with acetic anhydride–pyridine gave *p*-acetoxyphenetole (1·4 g.) as colourless plates, m. p. 54° (from light petroleum) (Found: C, 66·8; H, 6·8%).

(*b*) Similarly phenyl *iso*propyl ether (10·8 g.) with lead tetra-acetate (35 g.) in acetic acid (30 ml.) gave unchanged ether, n_D^{16} 1·4990, and p-*acetoxyphenyl* iso*propyl ether* (1·3 g.), b. p. 120°/3 mm. (Found: C, 68·2; H, 7·1. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%). No acetone was detected during the oxidation or the working-up.

Oxidation of Benzyl Phenyl Ether with Lead Tetra-acetate.—(*a*) Benzyl phenyl ether (14·8 g.) with lead tetra-acetate (37·6 g.) in acetic acid (80 ml.) was heated at 80° for 16 hr. Working up as for anisole (*a*) gave a yellow semisolid material, which by chromatography on alumina with light petroleum yielded unchanged benzyl ether (9·3 g.), m. p. and mixed m. p. 39—40°, and then p-*acetoxyphenyl benzyl ether* (0·8 g.), colourless plates, m. p. and mixed m. p. 110—111° (from aqueous ethanol) (Found: C, 74·2; H, 5·7. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%).

Quinol monobenzyl ether (0·3 g.; m. p. 122°) (Schiff and Pellizzari, *Annalen*, 1883, **221**,

370) with acetic anhydride–pyridine gave *p*-acetoxyphenyl benzyl ether (0·2 g.), colourless plates, m. p. 111° (from benzene–light petroleum) (Found: C, 74·5; H, 5·6%).

(*b*) Benzyl phenyl ether (14·8 g.) with lead tetra-acetate (37·6 g.) was oxidised as in (*a*) but for 12 hr. Excess of acetic acid was removed and the ether-soluble residue hydrolysed with aqueous sodium hydroxide. Steam-distillation of the alkaline solution gave benzaldehyde, isolated as the 2 : 4-dinitrophenylhydrazone (1·0 g., corresponding to 4·4% of α-phenoxybenzyl acetate), m. p. and mixed m. p. 238° (Found: N, 19·6. Calc. for $C_{13}H_{10}O_4N_4$: N, 19·6%). The acidified solution was extracted with ether, and the product, after removal of solvent, was chromatographed on alumina with light petroleum, giving unchanged benzyl phenyl ether (8·5 g.), m. p. and mixed m. p. 39—40°. Elution with chloroform yielded quinol monobenzyl ether (1·1 g.) as almost colourless plates, m. p. and mixed m. p. 121—122° (from water). In a further experiment phenol (from α-phenoxybenzyl acetate) was identified as 2 : 4 : 6-tribromophenol, colourless prisms, m. p. 93—94° (from aqueous methanol).

Oxidation of Benzyl p-*Tolyl Ether with Lead Tetra-acetate.*—Benzyl *p*-tolyl ether (7·0 g.; m. p. 41°) (Staedel, *ibid.*, 1883, **217**, 40) with lead tetra-acetate (15·9 g.) in acetic acid (40 ml.) was heated at 80° for 6 hr. The product (6·4 g.), worked up as above, was chromatographed on alumina. Elution with benzene–light petroleum (1 : 1) gave unchanged benzyl *p*-tolyl ether (3·4 g.), m. p. and mixed m. p. 40—41°, then chloroform yielded p-*benzyloxybenzyl alcohol* (2·8 g.), colourless plates, m. p. 88—89° (from ethyl acetate–light petroleum) (Found: C, 78·5; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%). Hydrogenation (Raney nickel) of this compound gave a quantitative yield of *p*-hydroxybenzyl alcohol, recrystallised as colourless needles, m. p. 110°, from water (Found: C, 67·7; H, 6·4. Calc. for $C_7H_8O_2$: C, 67·7; H, 6·5%). Auwers and Daecke (*Ber.*, 1899, **32**, 3373) record m. p. 124·5—125·5°; Sugimoto (*Reports Osaka Ind. Research Inst.*, 1929, **10**, No. 10; *Chem. Abs.*, 1930, **24**, 837) gives m. p. 110°.

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Kinetic Studies of the Oxidation of Aromatic Compounds by Potassium Permanganate. Part II. Substituted Toluenes.*

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A kinetic study has been made of the oxidation by potassium permanganate of some substituted toluenes. Oxidation is usually confined mainly to the methyl group which is converted into a carboxyl group, though with the xylenes and toluic acids considerable disruption of the aromatic ring also takes place. In general, the introduction of $+I$ substituents into toluene facilitates oxidation, while the presence of $-I$ groups decreases the ease of reaction.

Some of the compounds studied differ from toluene as regards the development of oxidation rate with time and the influence of reactant concentrations on the rate of reaction; possible explanations of the observed behaviour are discussed.

In Part I (Cullis and Ladbury, *J.*, 1955, 555) the results were presented of a kinetic study of the oxidation of toluene and related compounds by potassium permanganate. The present investigation deals with the oxidation of some substituted toluenes, and the behaviour of the nitro- and chloro-toluenes and of the toluic acids and xylenes is discussed.

Experimental

The experimental methods were similar to those described for toluene in Part I. The solvent was 54·2% w/v aqueous acetic acid in all cases.

Products of the Oxidation.—Full analyses were carried out with the xylenes (cf. Part I).

* Part I, *J.*, 1955, 555.

The only isolable products were the tolualdehydes and the toluic and phthalic acids corresponding to the original xylene. The acidic extracts gave, however, a faint red colour with diazotised *p*-nitroaniline; a side reaction involving hydroxyl radicals may evidently cause the production of small amounts of phenols (cf. Baxendale and Magee, *Discuss. Faraday Soc.*, 1953, **14**, 160).

o-Tolualdehyde gave a 2 : 4-dinitrophenylhydrazone of m. p. 193° (lit. 194°) which was shown not to be 2 : 4-dinitrophenylhydrazine (m. p. 198°) by mixed-m. p. depression (to 179°). *o*-Toluic acid and phthalic acid were separated by extraction of the former into chloroform. The recrystallised *o*-toluic acid had m. p. 104° and gave an amide of m. p. 141° (lit. 104°, 142°). Phthalic acid was identified by the fluorescein and the phenolphthalein colour reaction. *m*- and *p*-Tolualdehydes were converted into their 2 : 4-dinitrophenylhydrazones, m. p.s 90° and 233° (lit. 91°, 234°), respectively. *m*- and *p*-Toluic acids were separated from *iso*phthalic and terephthalic acids by extraction of the former compounds into benzene and ether, respectively. The toluic acids were identified by their m. p.s: *m*-toluic acid, 110° (lit. 110°); *p*-toluic acid, 179° (lit. 178°); and by conversion into their amides: *m*-toluamide, m. p. 96° (lit. 97°); *p*-toluamide, m. p. 157° (lit. 157°). *iso*Phthalic acid yielded an amide, m. p. 278° (lit. 280°), and terephthalic acid gave a dimethyl ester, m. p. 140° (lit. 140°).

Results and Discussion

Evolution of Carbon Dioxide.—During the oxidation of all the compounds studied carbon dioxide is evolved; this indicates that some disruption of the aromatic ring occurs simultaneously with side-chain oxidation. Some results of quantitative experiments with the isomeric xylenes and toluic acids are shown in Table 1.

Table 1

Temp.: 50°. [Organic compound] = 0·0103M; [$KMnO_4$] = 0·103M.

Compound	Compound completely oxidised (%)	Compound	Compound completely oxidised (%)
Toluene	7·0	*o*-Toluic acid	14·5
o-Xylene	26·9	*m*-Toluic acid	19·2
m-Xylene	41·8	*p*-Toluic acid	9·2
p-Xylene	57·0		

More ring rupture occurs with the xylenes than with the corresponding toluic acids and it is evident that fission of the ring must occur before the monocarboxylic acid is formed. This conclusion is in agreement with that reached with toluene, where it was shown that ring fission probably occurs at the alcohol and aldehyde stages (Cullis and Ladbury, *loc. cit.*).

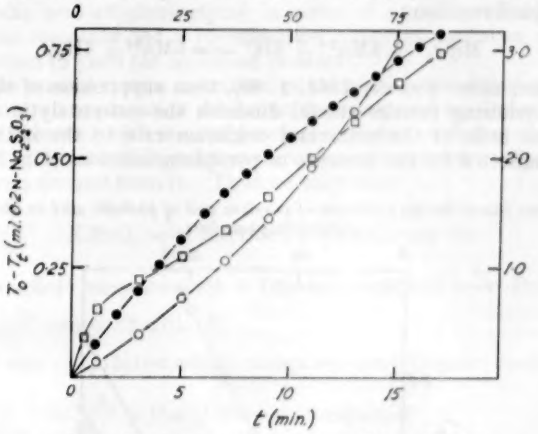
The fact that introduction of a methyl group into toluene increases the extent of disruption of the aromatic ring suggests that $+I$ substituents favour nuclear attack, and it might be expected that $-I$ substituents would exert a stabilising influence in this respect. This is in general true, though with the toluic acids the extent of nuclear attack is greater than with toluene itself. With nitro- and chloro-toluenes, nuclear attack is much reduced; quantitative estimates are difficult to obtain, since oxidation of these compounds is very slow and evolution of carbon dioxide from oxidative attack of the solvent and carboxylic acid " end-product " becomes appreciable.

The work of Speroni and Barchielli (*Gazzetta*, 1941, **71**, 765) suggests that with the chlorotoluenes no oxidative disruption of the aromatic ring takes place at any stage of the reaction unless sulphuric acid is present. The present results indicate that nuclear oxidation, though small, is not inappreciable; not only is carbon dioxide evolved during the oxidation, but chloride ions are formed.

The Development of Reaction with Time.—The course of the oxidation of the nitro- and chloro-toluenes and of *m*- and *p*-toluic acids is similar to that found with toluene. With some of the other compounds studied, *e.g.*, *m*- and *p*-xylene, the reaction–time curves are sigmoid in form, but with others, *e.g.*, *o*-xylene and *o*-toluic acid, oxidation takes place at an initially high rate and this is followed by a slow autocatalytic reaction (Fig. 1). The behaviour exhibited is thus similar to, but less pronounced than, that observed by Hinshelwood with *p*-nitrophenol (*J.*, 1919, 1180).

Study of the oxidation rates of *m*- and *p*-nitro- and of *m*- and *p*-chloro-benzoic acids and of *iso*phthalic acid (terephthalic acid could not be studied since it is almost insoluble in acetic acid) showed that the oxidation of these compounds is very slow. The oxidation

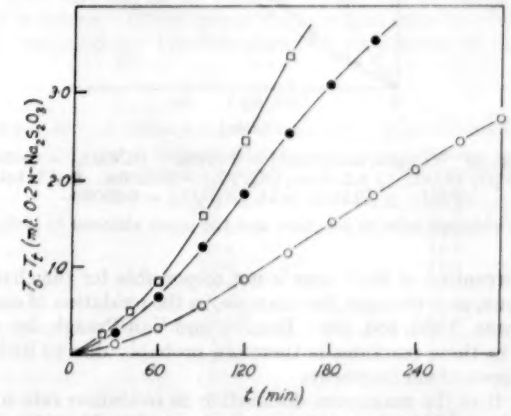
FIG. 1. *Reaction–time curves for the oxidation of* o- *and* p-*xylene and of* m-*toluic acid.*



○ Temp. 50°. [*p*-Xylene] = 0·0103M; [$KMnO_4$] = 0·00516M.
● Temp. 60°. [*m*-Toluic acid] = 0·0103M; [$KMnO_4$] = 0·0206M.
□ Temp. 50°. [*o*-Xylene] = 0·0103M; [$KMnO_4$] = 0·00516M.

The left-hand ordinates and lower abscissæ refer to *o*- and *p*-xylene; the right-hand ordinates and upper abscissæ to *m*-toluic acid. The ordinate values may be converted into "moles of $KMnO_4$ per litre" by multiplication by the factor $3·442 \times 10^{-3}$.

FIG. 2. *Reaction–time curves for the oxidation of* o-*substituted benzoic acids.*



Temp. 50°. [Organic compound] = 0·0103M.; [$KMnO_4$] = 0·0206M.
○ *o*-Nitrobenzoic acid; ● *o*-chlorobenzoic acid; □ phthalic acid.

of the three *ortho*-substituted benzoic acids, on the other hand, although initially slow, soon becomes appreciable (Fig. 2).

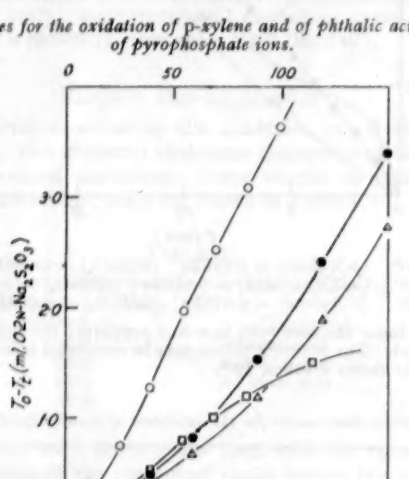
Sigmoid reaction–time curves are a common feature of reactions involving potassium permanganate, and may be due either to autocatalysis by Mn^{2+} ions (Bradley and van Praagh, *J.*, 1938, 1624; Alexander and Tompkins, *Trans. Faraday Soc.*, 1939, **35**, 1156) or to

fission of the compound undergoing oxidation (Hinshelwood and Winkler, *J.*, 1936, 368). Although the rate of reaction is reduced, the general form of such curves is not altered by allowing oxidation to proceed in presence of pyrophosphate ions (Fig. 3); these form a comparatively stable complex with the Mn^{3+} ion (Merz, Stafford, and Waters, *J.*, 1951, 638). If the sigmoid form of the reaction–time curves is due to autocatalysis by the Mn^{2+} ion as a result of the Guyard reaction:

$$MnO_4^- + 4Mn^{2+} + 8H^+ \longrightarrow 5Mn^{3+} + 4H_2O$$

(Guyard, *Bull. Soc. chim. France*, 1864, **1**, 89), then suppression of the above reaction as a source of oxidising entities should diminish the autocatalytic character of the curves. Since the ratio of the maximum oxidation rate to the initial oxidation rate is more or less unaffected by the presence of pyrophosphate ions (Fig. 3), it may be con-

FIG. 3. *Reaction–time curves for the oxidation of p-xylene and of phthalic acid in absence and in presence of pyrophosphate ions.*



Temp. 50°. [Organic compound] = 0·0103M.; $[KMnO_4]$ = 0·0206M.
○ *p*-Xylene, no $K_4P_2O_7$ added; □ *p*-Xylene, $[K_4P_2O_7]$ = 0·0206M; ● Phthalic acid, no $K_4P_2O_7$ added; △ Phthalic acid, $[K_4P_2O_7]$ = 0·0206M.

The lower abscissæ refer to *p*-xylene, and the upper abscissæ to phthalic acid.

cluded that the intervention of Mn^{2+} ions is not responsible for the characteristic development of rate with time, as is the case, for example, in the oxidation of oxalic acid (Harcourt and Esson, *Phil. Trans.*, 1866, **156**, 193; Bradley and Van Praagh, *loc. cit.*). The sigmoid form of the curves in these reactions is therefore probably due to fission of the ring and formation of labile open-chain fragments.

It is interesting that the maximum diminution in oxidation rate in presence of pyrophosphate ions is about 70% for *m*-xylene and about 50% for the *o*- and *p*-compounds; this suggests that the different oxidising species present effect a variable amount of oxidation depending on the substrate.

Influence of Reactant Concentrations.—With the chlorotoluenes (Speroni and Barchielli, *loc. cit.*), as with toluene itself (Cullis and Ladbury, *loc. cit.*), the initial rate of reaction is proportional to the first power of the concentrations of potassium permanganate and of the organic compound. With some of the substituted toluenes, second-order kinetics are no longer obeyed. The initial rates of oxidation of *m*- and *p*-xylene, for example, though

of the first order with respect to the oxidising agent, are somewhat less dependent on the xylene concentration.

Changes of the initial order with respect to the organic compound from unity to zero have previously been observed by Duke (*J. Amer. Chem. Soc.*, 1947, **69**, 2885, 3054), who suggests that such behaviour may be explained in certain systems, *e.g.*, manganic ions–oxalic acid, periodic acid–ethylene glycol, in terms of a rapidly established equilibrium between the initial reactants and a co-ordination complex, the latter undergoing a subsequent slow reaction to yield the oxidation products.

Although in the present system co-ordination between the oxidising agent and substrate is unlikely to occur, an explanation similar to that proposed by Duke may well account for the behaviour observed with *m*- and *p*-xylene. In the oxidation of toluene and other compounds studied here, it is believed that the principal oxidising entity is not the MnO_4^- ion but some species derived from it. Thus we may have :

$$KMnO_4 \underset{k_1'}{\overset{k_1}{\rightleftharpoons}} \text{Intermediate manganese ion} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\text{Intermediate manganese ion} + \text{Organic compound} \xrightarrow{k_2} \text{Products} \quad . \quad (2)$$

When (1) is rapid compared with (2),

$$\text{Initial rate} = k_2\,[\text{Intermediate manganese ion}]\,[\text{Organic compound}]$$

$$= \frac{k_1 k_2}{k_1'}\,[KMnO_4]\,[\text{Organic compound}]$$

and second-order kinetics are observed.

With more reactive compounds such as the xylenes (Table 2), reaction (2) may occur at a comparable rate to (1). In suitable circumstances reaction (1) may become rate-determining, and independence of rate on the concentration of the organic compound may be observed. Between the limits of applicability of these two rate laws there will be a range of concentrations where the order with respect to the organic compound lies between zero and unity. This may be, in its simplest terms, the explanation of the behaviour found with *m*- and *p*-xylene. Other special explanations may be advanced to account for the breakdown in second-order kinetics observed with some of the other compounds investigated.

TABLE 2

Temp. : 50°. [Organic compound] = 0·01M. ; $[KMnO_4]$ = 0·02M.

Compound	$10^5 \times$ Initial oxidation rate (mole $l.^{-1}$ $min.^{-1}$)	E (kcal. $mole^{-1}$)	A ($l.$ $mole^{-1}$ $min.^{-1}$)
Toluene	15·7	13·2	$6{\cdot}45 \times 10^8$
o-Xylene	110	10·3	—
m-Xylene	96·6	13·0	—
p-Xylene	49·6	13·2	—
o-Toluic acid	13·9	14·9	$7{\cdot}93 \times 10^9$
m-Toluic acid	8·44	13·9	$9{\cdot}95 \times 10^8$
p-Toluic acid	7·46	13·2	$3{\cdot}24 \times 10^8$
o-Nitrotoluene	0·72	13·8	$7{\cdot}41 \times 10^7$
m-Nitrotoluene	1·15	11·8	$5{\cdot}83 \times 10^8$
p-Nitrotoluene	2·44	14·7	$9{\cdot}61 \times 10^8$
o-Chlorotoluene	2·86	13·8	$2{\cdot}93 \times 10^8$
m-Chlorotoluene	4·96	15·7	$1{\cdot}03 \times 10^{10}$
p-Chlorotoluene	5·16	14·6	$2{\cdot}01 \times 10^9$
o-Nitrobenzoic acid	0·6	—	—
o-Chlorobenzoic acid	1·7	—	—
Phthalic acid	2·8	—	—
Benzoic acid	0·6	11·8	$2{\cdot}76 \times 10^8$

Influence of Structure.—The initial rates of oxidation of the compounds studied are shown in Table 2, together with the Arrhenius parameters in certain cases; the rates given are corrected for oxidative attack of the solvent.

The order of ease of oxidation of the nitro- and chloro-toluenes is : $H > p > m > o$,

while with the toluic acids the order is: $H > o > m > p$. For the xylenes, the sequence is: $o > m > p > H$. The same order of rates of oxidation is found with the *ortho*-substituted benzoic acids as with the *ortho*-substituted toluenes, *i.e.*, $CO_2H > Cl > NO_2$, but *o*-nitrobenzoic acid is oxidised at the same initial rate as benzoic acid, while toluene reacts about twenty times as fast as *o*-nitrotoluene. The results in Table 2 show that such variations in rate as occur when the position of a given substituent is altered are due to changes in both the Arrhenius parameters, E and A. The general effect of substitution is evidently quite complex and it is not surprising that structural changes affect the values of E and A to different extents, and hence give different sequences of ease of oxidation according to the nature of the substituent.

In general, however, the introduction of $-I$ substituents into toluene decreases the oxidisability, while $+I$ substituents facilitate oxidation. This suggests that the oxidising agent is a cationic species such as Mn^{3+} and not a free radical, for in reactions involving the attack of aromatic molecules by radicals there is evidence that both $+I$ and $-I$ groups exert an activating influence (Dewar, "Electronic Theories of Organic Chemistry," Oxford University Press, 1949, p. 278; De Tar and Scheifele, *J. Amer. Chem. Soc.*, 1951, **73**, 1442; Hey, *J.*, 1952, 1974).

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Mesomorphism and Chemical Constitution. Part V. The Mesomorphic Properties of the 4'-n-Alkoxydiphenyl-4-carboxylic Acids and their Simple Alkyl Esters.*

By G. W. Gray, J. B. Hartley, and Brynmor Jones.

[Reprint Order No. 5878.]

Thirteen 4'-*n*-alkoxydiphenyl-4-carboxylic acids have been prepared and their mesomorphic behaviour is compared with that of the 4-*n*-alkoxybenzoic acids. They exhibit mesophases of much greater relative thermal stability than the simpler benzoic acids; this is attributed to the enhanced intermolecular cohesion arising from the second aromatic ring and to the greater molecular length of the diphenyl compounds. The high relative thermal stability of the mesophases is emphasised by the mesomorphic behaviour of the methyl, ethyl, and *n*-propyl alkoxydiphenylcarboxylates, and the absence of anisotropic melts in the analogous alkoxybenzoates.

In order to establish whether certain diphenyl compounds can exhibit mesomorphism, some thirteen 4'-*n*-alkoxydiphenyl-4-carboxylates have been prepared. All have anisotropic melts, and the relative thermal stabilities of their mesophases are much higher than those of other mesomorphic compounds examined hitherto. The melting points and mesomorphic transition temperatures are summarised in Table 1, and in Fig. 1 the latter are plotted against the number of carbon atoms in the alkyl chain.

Although all thirteen ethers are mesomorphic, the first four alone possess purely nematic properties, but in the pentyl ether an additional, short, enantiotropic smectic phase appears. Thereafter, there is a gradual increase in smectic phase length and in the smectic–nematic transition temperature, which reaches its maximum at 256·5° in the nonyl and decyl ethers. At the same time there is a gradual decrease in nematic phase length, until, in the dodecyl, hexadecyl, and octadecyl ethers, purely smectic properties are encountered. It is clear from Fig. 1 that the mesomorphic–isotropic transition temperatures exhibit the usual alternations associated with homologous series of mesomorphic ethers containing alkyl chains made up of odd and even numbers of carbon atoms.

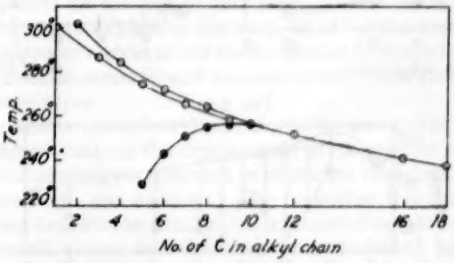
* Part IV, *J.*, 1955, 236.

Hence, these transition points lie on two falling curves, the upper one determined by those ethers containing an even number, and the lower by those with an odd number of carbons in the alkyl chain. As a result of this alternation, the highest mesomorphic–isotropic transition temperature is 301·5°—found for the nematic–isotropic change in the ethyl ether. The smectic–nematic transition points also lie on a smooth curve (Fig. 1), which, after an initial rise, levels off for the nonyl and decyl ethers. The curve is then drawn to

TABLE 1. 4′-n-*Alkoxydiphenyl-4-carboxylic acids*, 4′-RO·C_6H_4·C_6H_4·CO_2H-4 (I).

R in (I)	Temp. of transition to smectic	nematic	iso-tropic	Phase length of smectic	nematic	R in (I)	Temp. of transition to smectic	nematic	iso-tropic	Phase length of smectic	nematic
Me	—	258°	300°	—	42°	C_8H_{17}	183°	255°	264·5°	72°	9·5°
Et	—	256·5	301·5	—	45	C_9H_{19}	176	256·5	258·5	80·5	2
Pr	—	260	287	—	27	$C_{10}H_{21}$	172·5	256·5	257	84	0·5
Bu	—	234	284·5	—	50·5	$C_{12}H_{25}$	165	—	252	87	—
C_5H_{11}	227·5°	229·5	275	2°	45·5	$C_{16}H_{33}$	151	—	241·5	90·5	—
C_6H_{13}	213	243	272·5	30	29·5	$C_{18}H_{37}$	150	—	238	88	—
C_7H_{15}	194·5	251	265·5	56·5	14·5						

FIG. 1.



coincide with the mesomorphic–isotropic transition point curve for members containing an even number of carbons in the alkyl group, since the decyl ether is the last to exhibit a nematic phase. In their general characteristics, the 4′-alkoxydiphenyl-4-carboxylic acids constitute a typical homologous series of mesomorphic compounds, similar to other series of alkoxyarenecarboxylic acids which have been examined previously (Gray and Brynmor Jones, *J.*, 1953, 4179; 1954, 683, 1467). With all these carboxylic acids (and these include the *p*-alkoxybenzoic acids, the *trans*-*p*-alkoxycinnamic acids, and the 6-alkoxy-2-naphthoic acids), the esters showed no mesomorphism. This probably arises from their inability to form a dimerised molecule, which is most probably the effective unit in the mesophases of the acids—and the cohesive forces which exist between the shorter, monomeric ester molecules are insufficient to allow of the existence of a mesophase. In view of the high relative thermal stability of the diphenylcarboxylic acids, it seemed possible that their alkyl esters, the alkyl 4′-alkoxydiphenyl-4-carboxylates, would be mesomorphic, since both their length and the intermolecular cohesion will be greater than those of the alkyl 4-alkoxybenzoates or the alkyl 6-alkoxy-2-naphthoates. The methyl, ethyl, and *n*-propyl esters of all thirteen 4′-alkoxydiphenyl-4-carboxylic acids were therefore prepared and examined, and in many cases mesomorphic phases were found. The m. p.s and smectic–isotropic transition temperatures (*T*) for these esters are summarised in Table 2, and in Fig. 2 (*a*)—(*c*) these are plotted against the number of carbon atoms in the alkoxy-group.

It is significant that the esters exhibit only smectic phases, and that in the three series of methyl, ethyl, and propyl esters the first members to be mesomorphic are the hexyl, pentyl, and ethyl ethers, respectively. The smectic–isotropic transition temperatures for the methyl esters fall as the alkyl chain length is increased, and, although only two of the ethers containing an odd number of carbon atoms are mesomorphic, the usual alternation of the transition points is evident. The transition temperatures for the even carbon chain ethers (hexyl–octadecyl) lie on a smooth, falling, curve, whilst those for the heptyl and nonyl ethers lie slightly below and on this curve, respectively, and constitute what is no doubt the end of a lower curve, whose exact position would be determined by the methyl,

propyl, and pentyl ethers had they too been mesomorphic. In Fig. 2(*a*), these curves are extrapolated towards the shorter carbon chain lengths to show that the intercepts lie well below the m. p.s, and that phases are not observed in the methyl–pentyl ethers.

The hexadecyl and octadecyl methyl esters exhibit monotropic mesomorphism when the isotropic liquid is cooled—the isotropic–smectic reversal temperature was readily obtained for the hexadecyl ether, but, with the octadecyl ether, unless the isotropic liquid was chilled rapidly, crystallisation occurred before the phase appeared. Although no accurate reversal point for this monotropic phase could therefore be obtained, extrapolation of the smectic–isotropic transition point curve for even carbon chain ethers indicates that the value should be about 112·5° [Fig. 2(*a*)].

FIG. 2 (*a*).

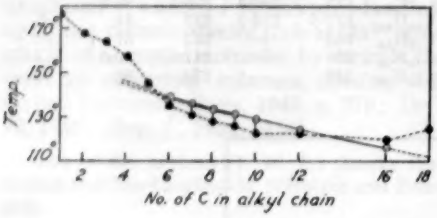


FIG. 2 (*b*).

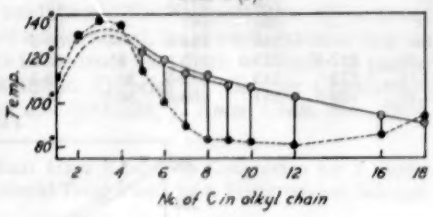


FIG. 2 (*c*).

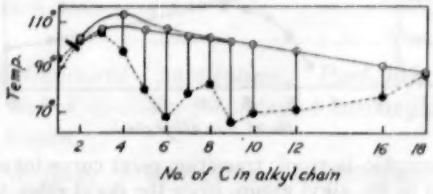


TABLE 2. *Alkyl 4′-alkoxydiphenyl-4-carboxylates*, 4′-RO·C_6H_4·C_6H_4·CO_2R′-4 (II).

R in (II)	R = Me M. p.	*T*	R′ = Et M. p.	*T*	R′ = Pr[a] M. p.	*T*	R in (II)	R′ = Me M. p.	*T*	R′ = Et M. p.	*T*	R′ = Pr[a] M. p.	*T*
Me	176·5°	—	112°	—	94°	—	C_8H_{17}	127·5°	133·5°	83·5°	112°	82·5°	103°
Et	167·5	—	131	—	102	103°	C_9H_{19}	126	131	83	108	64·5	101
Pr	164	—	137·5	—	105	107	$C_{10}H_{21}$	122·5	128·5	82	107	69·5	100
Bu	157	—	135	—	97	113·5	$C_{12}H_{25}$	122·5	124	80·5	102·5	71	97
C_5H_{11}	145	—	114·5	123·5°	80	106·5	$C_{14}H_{29}$	119·5	(116) *	85·5	94	76·5	90·5
C_6H_{13}	134·5	139°	100·5	119·5	67·5	107	$C_{16}H_{33}$	125	(<121·5) *	93·5	(90·5) *	86·5	87·5
C_7H_{15}	130·5	135·5	89·5	113·5	78	103·5							

* Monotropic transition temperatures are in parentheses.

In the ethyl esters, the alternation in the smectic–isotropic transition points is more noticeable, and two distinct curves are produced for the members of the series containing odd and even numbers of carbon atoms. Here, only the octadecyl ether exhibits a monotropic phase, whose isotropic–smectic reversal was readily determined by cooling the melt slowly. The distribution of the m. p.s of the first four non-mesomorphic ethyl esters is interesting, since they rise to a maximum at propyl and then fall to butyl. Therefore, if the smectic–isotropic transition-point curves [Fig. 2(*b*)] for the ethyl esters are extrapolated backwards in such a way that they conform to the shape of a normal nematic–isotropic transition point curve (Fig. 1), the methyl and ethyl ethers, and probably the propyl and butyl ethers too, should exhibit enantiotropic smectic phases. Since these are not in fact observed, it must be inferred that these m. p.s are higher than the maximum temperatures at which mesophases could exist in these ethers; *i.e.*, their " mesophases," if they could be detected, would be monotropic. They fail to appear because the isotropic liquids do not supercool sufficiently before crystallisation occurs. The inference is that these " monotropic points " (isotropic–smectic) lie below the m. p.s in each case, so that the complete smectic–isotropic transition point curve can be envisaged only by extrapolation

(broken curves) as shown in Fig. 2(*b*). The precise shapes of these portions of the curve are of course conjectural but, both for the odd and even members, some such curve, which rises to a maximum and then falls through the experimentally determined enantiotropic points, is indicated. It is legitimate to draw these broken curves quite close to the actual m. p.s, because the isotropic melts of the ethyl–butyl ethers crystallise within 0·5° of their m. p.s, and that of the methyl ether at 108°, only 4° below the m. p.

It may be that the same state of affairs obtains in the methyl esters, but here, because of the steady fall in m. p. from the methyl ether to the first mesomorphic member, there is no evidence to suggest that this is the case. However, the propyl esters provide evidence that a smectic–isotropic transition point curve can rise to a maximum and then fall. This is apparent from Fig. 2(*c*), where a steep rise in smectic–isotropic transition temperature is indicated on passing from the ethyl to the butyl ether, and this in turn is followed by a gradual decrease along the remainder of the ethers which have even numbers of carbons in the alkoxy-group. Further, the smectic–isotropic transition point (107°) for the propyl ether is only slightly higher than that of the pentyl ether (106·5°), and it would appear that these two points define the optimum portion of a similar curve which lies below the first, and falls through the points for the heptyl and nonyl ethers. This curve has again been extrapolated (broken curve) to fall below the m. p. of 94° of the non-mesomorphic methyl ether. Such smectic–isotropic curves are of course similar in shape to the curve which may be drawn through the smectic–nematic and smectic–isotropic points in a homologous series which exhibits both phase types.

In the case of an alkoxyarenecarboxylic acid which can exhibit both a smectic and a nematic phase, it is evident that, as the temperature of its smectic phase is raised, a stage is reached when the thermal energy is sufficient to overcome the lateral cohesive forces which keep the molecules parallel to one another. The molecules therefore are free to slide in the direction of their long axes and so produce an imbricated nematic melt. The molecular orientation in the nematic phase will therefore be maintained by the residual lateral cohesions and by the terminal cohesive forces between molecules arranged end-to-end. In the 4′-alkoxydiphenyl-4-carboxylic acids, and in other homologous series which have been examined, the smectic–nematic transition points lie on a curve which rises steeply at first and then levels off as the alkyl chain is lengthened. This effect must be related to an increase of the same order in the lateral cohesive forces. On the other hand, the falling curve on which the nematic–isotropic transitions lie may be accounted for if the overall cohesion arising from the terminal and residual lateral cohesions decreases as the alkyl chain is extended. The alternations in the mesomorphic–isotropic transition temperatures may result from differences in packing and cohesion between the terminal methyl groups of alkyl chains containing odd and even numbers of carbon atoms. Such an explanation was originally suggested by Malkin (*Trans. Faraday Soc.*, 1933, **29**, 977) to account for the alternation of m. p.s in homologous series. Since the cohesive forces which determine the nematic–isotropic change decrease as the chain length grows, whilst the lateral cohesions determining the smectic–nematic change increase and then level off, a stage will be reached when the terminal cohesions, which must be the decreasing component of the overall cohesions in the nematic phase, become so weak that they may well determine the mesomorphic–isotropic change before sliding takes place. When this occurs, no nematic phase should appear, and the smectic phase must be imagined as passing direct to the isotropic liquid as a result of breakdown of the cohesion between the orientated layers of the phase. In this way, the occurrence of purely smectic properties in the longer-chain members of a series can be understood, and also the fact that the nematic and smectic–isotropic transitions fall on one curve for the even carbon chain ethers. At the other end of the series, the shorter molecules are usually purely nematic, presumably because their lateral cohesions are so low that, when the solid melts, the molecules also slide along their long axes without producing a smectic phase. On the basis of these arguments, it seems probable that a compound will exhibit purely smectic properties when the lateral cohesive forces are relatively much greater than the terminal cohesions. Such a condition does obtain in the alkyl 4′-alkoxydiphenyl-4-carboxylates (II). Here, the resultant dipole of the ethoxycarbonyl group, which acts across the molecule, will make a considerable

contribution to the lateral cohesions between molecules in a smectic layer packing—in which the molecules lie parallel to one another, with their ends in line. In a dimerised carboxylic acid there is, of course, no such effect to increase the lateral cohesions. The dipole which acts across a molecule's long axis has already been shown to increase the stability of a smectic phase to a much greater extent than a nematic phase (Part IV, *loc. cit.*).

For example, the increase in relative thermal stability of the nematic phase in passing from 6-octyloxy-2-naphthoic acid to its 5-chloro-derivative, in which the dipole again acts across the molecule's long axis, is only 7·5°, whereas the relative stability of the smectic phase increases by 20°. (As explained in Part IV, *loc. cit.*, it is realised throughout this paper that mesomorphic temperatures are only an *indication* of relative thermal stability and are not a *measure* of stability.) Both these effects are presumably brought about by the C–Cl dipole moment. The 5-bromo- and 5-iodo-6-alkoxy-2-naphthoic acids illustrate the same effect, while the 5-nitro-compounds, containing the larger C–NO_2 dipole, exhibit only smectic properties. The alkyl esters appear therefore to have the same characteristics as those compounds which are either purely smectic or exhibit smectic phases of relatively high thermal stability.

In the light of the preceding discussion, we now review the shape of the smectic–isotropic transition point curve in the propyl esters. In the esters which contain a short alkoxy-group, the transition temperature from the smectic phase to the isotropic liquid is probably determined by the loosening of the lateral cohesive forces. Since no nematic phase is exhibited, it seems likely that the terminal cohesions are not sufficiently strong to maintain the order in a nematic phase, and these cohesions presumably are weakened at the same time as the lateral cohesions. The lateral attractive forces between molecules increase as the alkyl-chain length grows, with the result that the smectic–isotropic transition temperatures like the smectic–nematic changes would be expected to rise, *e.g.*, from ethoxy- to butyloxy- in the propyl esters. However, the increase in lateral cohesions is accompanied by a decrease in the already relatively small terminal attractions. At a certain alkyl-chain length (pentyl in this series) the weakness of these terminal cohesions may begin to determine when the phase becomes isotropic by permitting the individual layers in the smectic packing to move apart and, ultimately, to result in a condition of isotropy. At the pentyl ether, the smectic–isotropic transition temperatures should begin to decrease. The relative strengths of the lateral and terminal cohesions will determine the precise position in a series at which the maximum smectic–isotropic transition temperature is found, or, indeed, whether such a maximum will appear at all. That terminal cohesions do play a part in determining these transitions is shown by the alternation of smectic–isotropic transition temperatures between members containing odd and even numbers of carbon atoms in the alkoxy-group. The smectic–nematic transition points do not alternate, since this change is determined by a sliding of the molecules when the lateral cohesions become sufficiently reduced by the thermal energy supplied.

A homologous series of alkyl esters of one particular 4-*n*-alkoxydiphenyl-4-carboxylic acid would constitute another potential series of mesomorphic esters. Since increments in the length of the ester alkyl group would produce the same effects as lengthening the alkoxy-group, it is likely that the behaviour of such a series would be similar to that of the present methyl, ethyl, or propyl esters. A complete series of this kind has not been prepared, but if the m. p.s and smectic–isotropic transition points for the methyl, ethyl, and propyl esters of each individual alkoxy-compound are plotted in turn against the number of carbon atoms in the ester chains, the relative behaviour of the first three members of the various series can be established. The changes from methyl to ethyl to propyl ester indicate that the graphs would be similar to those obtained for the complete series of methyl esters [Fig. 2(*a*)], and would give no further evidence for the smectic–isotropic transition-point curve of the type found for the propyl esters [Fig. 2(*c*)]. In any one set of three homologous, mesomorphic esters, the decrease in smectic–isotropic transition temperature is greater from methyl to ethyl than from ethyl to propyl. In a complete series of homologous alkyl esters, an alternation of this type would mean that the smectic–isotropic transitions for the odd carbon chain esters (methyl, propyl, etc.) would lie on one curve,

and those for the even chain esters on a lower curve. The opposite effect of odd–even alternation is always observed in homologous series of alkoxy-compounds, where the ethers containing an even number of carbon atoms in the alkyl chain give transition points which constitute the upper of the two curves (cf. Fig. 1). This difference is readily explained, because a methoxy-group, with its one carbon atom, may be considered equivalent to an ethyl group containing two carbon atoms, since the oxygen atom affects the length of the chain, and the orientation of the terminal methyl group, almost exactly as a carbon atom would do. Hence, an alkyl ester with an even number of carbon atoms gives the same orientation of its terminal methyl group as an alkyl ether with an odd number of carbon atoms in the alkyl chain. This effect has already been observed by Weygand and Gabler (*Z. physikal. Chem.*, 1940, **46**, *B*, 270) in the *p*-*n*-alkylbenzoic acids, which are purely nematic in character. The nematic–isotropic transition points for these acids alternate appreciably and, in contrast to the *p*-*n*-alkoxybenzoic acids (Gray and Brynmor Jones, *J.*, 1953, 4179), are considerably higher for the odd members (pentyl–nonyl) than for the even carbon chain compounds (butyl–decyl).

As already mentioned, the 4′-alkoxydiphenyl-4-carboxylic acids exhibit a relative mesomorphic stability which is much greater than in any series so far encountered. The extent of this effect is made clear by comparison with the *p*-alkoxybenzoic acids. Table 3 summarises the average mesomorphic–isotropic transition temperature for propyl–octadecyl (A), the average smectic–nematic transition temperature for heptyl–decyl (B), and the average smectic–nematic and smectic–isotropic transition temperature for heptyl–octadecyl (C) of the *p*-alkoxybenzoic and 4′-alkoxydiphenyl-4-carboxylic acids.

TABLE 3.

Average transition type	*p*-RO·C_6H_4·CO_2H	4′-RO·C_6H_4·C_6H_4·CO_2H-4	Increase in relative thermal stability
A	145·1°	263·3°	118·2°
B	111·25	254·75	143·5
C	119·6	250·1	130·5

The molecule of the monomer of the diphenyl acid is longer because of the second aromatic ring, which, as a result of its polarisability, increases the intermolecular cohesive forces. The mesophases of the diphenyl acids would be expected therefore to exhibit a greater relative thermal stability. Moreover, the second aromatic ring probably increases the lateral cohesions to a greater extent than the terminal cohesions. Compared with the benzoic acids, the smectic phases of the diphenyl acids should show a greater increased relative stability than the nematic phases. This effect is, in fact, found. Comparison of the heptyl–decyl ethers in each case shows that the average relative stability of the smectic phases in the diphenyl acids is greater by 143·5°, whilst the relative nematic stability is higher by only 116·9°.

When these relative stability effects are taken into account it is not surprising that the alkyl *p*-alkoxybenzoates are not mesomorphic, for their relative mesomorphic stabilities would be much lower than those of the alkyl 4′-alkoxydiphenyl-4-carboxylates. The average smectic–isotropic transition temperatures for all enantiotropic mesomorphic members in the methyl, ethyl, and propyl esters of the diphenyl acids are 131·9°, 110°, and 101·6° respectively. Therefore, if the same degree of decrease in relative stability, found in passing from the diphenyl acids to the benzoic acids occurs in the esters, the " mesomorphic–isotropic transitions " of the alkyl *p*-alkoxybenzoates would take place at temperatures below 0°, and certainly at temperatures substantially less than the m. p.s of the esters.

EXPERIMENTAL

M. p.s are corrected.

The mesomorphic and polymorphic transitions were determined in an electrically heated block (Gray, *Nature*, 1953, **172**, 1137). The enantiotropic mesomorphic changes were measured in the usual way : all values except those from the solid to the mesophase were checked both by heating and by cooling the specimen. In the case of the diphenyl acids, the changes observed in polarised light were from the solid to the fine mosaic of smectic focal-conics, from the solid or smectic phase to the mobile, threaded nematic phase, and from the solid or mesophase to the

extinct isotropic liquid. In many cases the temperatures of transition are high, and frequently the sample under observation underwent rapid sublimation. This was reduced by using a freshly mounted sample for the determination of each transition, and by raising the temperature of the block to within 10° of the expected transition before inserting the slide, the approximate transition point having previously been determined in a m. p. capillary. The alkyl esters exhibit no nematic phase, but their smectic phases appear in clearly defined focal-conic groups which are frequently maintained when the solid is obtained by cooling from the mesophase. This pseudomesomorphic condition frequently makes it difficult to observe the change of the solid to the smectic phase, but the disappearance of cleavage lines in the solid can, with care, be used as a reliable indication of the occurrence of the transition. The reversal from the isotropic liquid to the mesophase is characterised by the appearance of typical bâtonnets which coalesce to the focal-conic pattern. Several of the esters exhibit monotropic smectic properties, and these transitions were determined by carefully observing the isotropic liquid as it cooled slowly until the bâtonnets appeared. It was sometimes possible to raise the temperature, while the specimens were in these monotropic states, without inducing crystallisation, and thus to obtain the transition temperature in reverse. Good agreement was found with the values obtained on cooling. In the case of methyl 4′-octadecyloxydiphenyl-4-carboxylate, the low rate of cooling (about 1° per min.), which was necessary for accurate measurement of the transitions, was too slow, and crystallisation occurred. Here, the value for the isotropic–smectic reversal temperature was obtained only by extrapolation of the curve constructed from experimentally determined values for the other members of the series.

Polymorphic Transition Temperatures.—See following Table. Here solid I is the stable solid at room temperature. No polymorphism was observed in the 4′-alkoxydiphenyl-4-carboxylic acids.

Solid I–*solid* II *transition temperatures in* $RO{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}CO_2R'$.*

R	R′ = Me	R′ = Et	R′ = Pr	R	R′ = Me	R′ = Et	R′ = Pr
Me	—	—	*	C_7H_{15}	120·5°	52°	—
Et	—	*	*	C_8H_{17}	120·5	58	—
Pr	—	98°	71°	C_9H_{19}	122·5	53	—
Bu	138°	*	56	$C_{10}H_{21}$	121	59	67°
C_5H_{11}	122·5	41	68·5	$C_{18}H_{35}$	*	75	*
C_6H_{13}	123	50	59				

* The esters so denoted exhibit a monotropic form.

Preparation of Materials.—*4-Methoxydiphenyl.* 4-Hydroxydiphenyl (85 g., 1 mol.), dissolved in hot 1·5N-sodium hydroxide (1·5 l.), was treated with methyl sulphate (2 mols.) so that the temperature did not exceed 60°. The temperature was then raised to 70° for 30 min. The product crystallised from ethanol as colourless plates, m. p. 80·5° (90—95%).

4-Acetyl-4′-methoxydiphenyl. Crystallised 4-methoxydiphenyl (11·5 g., 1 mol.) was dissolved in dry, redistilled carbon disulphide (75 ml.), contained in a three-necked flask, equipped with stirrer, dropping-funnel, and condenser. The solution was cooled to 0—2°, and sieved, anhydrous aluminium chloride (9·5 g., 1·12 mol.) was added quickly, with stirring. Acetyl chloride (5·8 ml., 1 mol.) was then added during 5—10 min., and the temperature raised gradually to 35°. The mixture was kept at 35° until the reaction seemed to be over, whereupon the whole was refluxed for 45 min. Ice-cold, concentrated hydrochloric acid (60 ml.) was then added to the cooled mixture to decompose the yellow-green complex. The condenser was removed, and steam passed under the surface of the solution to remove the solvent and complete the decomposition of the complex. Stirring was continued as the mixture was cooled quickly, in order to obtain the brownish-pink solid in a finely divided state. The solid was separated, dried, and triturated twice by stirring for 15 min. with ether (40 ml.). The insoluble 4′-acetyl derivative was thus separated from the isomeric 3-ketone, which is soluble in ether. The 4-acetyl-4′-methoxydiphenyl crystallised from *iso*propyl alcohol as colourless flakes, m. p. 156·5°. Johnson, Gutsche, and Offenhauer (*J. Amer. Chem. Soc.*, 1946, **68**, 1649) gave m. p. 153—154°. The yield varied between 25 and 60%. However, when the aluminium chloride was dried for several hours at 100—120°, and the amounts of acetyl chloride and aluminium chloride were increased to 1·1 and 1·17 mol., respectively, the yields were 60—77% in three consecutive preparations.

4′-Methoxydiphenyl-4-carboxylic acid. The foregoing compound was oxidised by aqueous sodium hypobromite, as described by Johnson, Gutsche, and Offenhauer (*loc. cit.*), although a more dilute solution of the ketone in dioxan was used (18 g. in 285 ml.). The crude product

(95% yield), crystallised from ethyl alcohol and acetic acid, had m. p. 258° (75—85%). Johnson *et al.* give m. p. 248—249°.

4'-Hydroxydiphenyl-4-carboxylic acid. The methyl ether (25 g.), acetic acid (1 l.), and 48% hydrobromic acid (200 ml.) were refluxed for 12—14 hr., then poured into water (2·5 l.) and cooled, and the precipitate was separated. The dried material, m. p. 288—291° (90—95%), was not quite pure, but the m. p. could not be improved by repeated crystallisation or by chromatography. The product was, however, satisfactory for the preparation of the alkyl ethers. A pure sample of the hydroxy-compound (Found: C, 72·7; H, 4·66. Calc. for $C_{13}H_{10}O_3$: C, 72·9; H, 4·67%), m. p. 294·5°, was obtained by hydrolysing the purified *acetyl* derivative (Found: C, 70·2; H, 4·7. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%), m. p. 260—262° (decomp.), obtained from the crude hydroxy-compound by acetylation and crystallisation once from glacial acetic acid, once from xylene, and twice from ethyl acetate. The acetyl derivative is mesomorphic. Fieser and Bradscher (*J. Amer. Chem. Soc.*, 1936, **58**, 1738) claim that the hydroxy-compound can be purified by crystallisation from dioxan–*cyclo*hexane, and give m. p. 293—294°, but, although this procedure was tried, no improvement in the m. p. of the crude product was observed.

4'-n-Alkoxydiphenyl-4-carboxylic acids. The hydroxy-acid (0·01 mole) and potassium hydroxide (0·02 mole) were dissolved in hot alcohol (300 ml.) and water (30 ml.). The *n*-alkyl halide (1·2 moles) was then added, and the mixture refluxed for 12 hr. Any ester formed during alkylation was hydrolysed by adding a 10% solution of potassium hydroxide (0·02 mol.) in 70% ethanol and refluxing for a further 2 hr. The *alkoxy-acids* (see Table) crystallised from glacial acetic acid, and at this stage the yields were 85—90%. The products were then crystallised from ethyl alcohol and glacial acetic acid alternately until no alteration in their physical constants (Table 1) was observed.

4'-n-Alkoxydiphenyl-4-carboxylic acids.

	Found (%)		Required (%)				Found (%)		Required (%)		
Alkyl	C	H	Formula	C	H	Alkyl	C	H	Formula	C	H
* Methyl ...	73·7	5·3	$C_{14}H_{12}O_3$	73·7	5·3	Octyl	77·3	7·9	$C_{21}H_{26}O_3$	77·2	8·0
Ethyl	74·5	5·6	$C_{15}H_{14}O_3$	74·4	5·8	Nonyl	77·5	8·2	$C_{22}H_{28}O_3$	77·6	8·3
Propyl ...	74·8	6·1	$C_{16}H_{16}O_3$	74·9	6·3	Decyl	76·7	8·3	$C_{23}H_{30}O_3$	77·9	8·5
Butyl	75·3	6·5	$C_{17}H_{18}O_3$	75·5	6·7	Dodecyl ...	78·5	8·9	$C_{25}H_{34}O_3$	78·5	9·0
Pentyl ...	76·0	7·1	$C_{18}H_{20}O_3$	76·0	7·1	Hexadecyl	79·5	9·6	$C_{29}H_{42}O_3$	79·4	9·65
Hexyl ...	76·5	7·5	$C_{19}H_{22}O_3$	76·5	7·4	Octadecyl ...	79·6	9·9	$C_{31}H_{46}O_3$	79·8	9·9
Heptyl ...	76·8	7·7	$C_{20}H_{24}O_3$	76·9	7·7						

* Not new.

Alkyl 4'-alkoxydiphenyl-4-carboxylates. The *methyl*, *ethyl*, and n-*propyl* esters (see following Table) were prepared in the usual way from the appropriate alcohol and concentrated sulphuric

	Found (%)		Required (%)				Found (%)		Required (%)		
Alkyl	C	H	Formula	C	H	Alkyl	C	H	Formula	C	H
Methyl 4'-alkoxydiphenyl-4-carboxylates.											
Me	74·4	5·9	$C_{15}H_{14}O_3$	74·4	5·8	C_8H_{17} ...	77·6	8·2	$C_{22}H_{28}O_3$	77·6	8·3
Et	75·0	6·3	$C_{16}H_{16}O_3$	74·9	6·3	C_9H_{19} ...	78·1	8·5	$C_{23}H_{30}O_3$	77·9	8·5
Pr	75·7	6·8	$C_{17}H_{18}O_3$	75·5	6·7	$C_{10}H_{21}$ ...	78·4	8·7	$C_{24}H_{32}O_3$	78·3	8·7
Bu	76·0	7·0	$C_{18}H_{20}O_3$	76·0	7·1	$C_{12}H_{25}$ ...	78·8	9·0	$C_{26}H_{36}O_3$	78·8	9·1
C_5H_{11} ...	76·6	7·3	$C_{19}H_{22}O_3$	76·5	7·4	$C_{16}H_{33}$ ...	79·8	9·8	$C_{30}H_{44}O_3$	79·65	9·7
C_6H_{13} ...	76·9	7·8	$C_{20}H_{24}O_3$	76·9	7·7	$C_{18}H_{37}$ ...	80·1	10·0	$C_{32}H_{48}O_3$	80·0	10·0
C_7H_{15} ...	77·3	8·0	$C_{21}H_{26}O_3$	77·2	8·0						
Ethyl 4'-alkoxydiphenyl-4-carboxylates.											
Me	75·0	6·2	$C_{16}H_{16}O_3$	74·9	6·3	C_8H_{17} ...	78·1	8·4	$C_{23}H_{30}O_3$	77·9	8·5
Et	75·4	6·8	$C_{17}H_{18}O_3$	75·5	6·7	C_9H_{19} ...	78·3	8·7	$C_{24}H_{32}O_3$	78·3	8·7
Pr	76·1	6·9	$C_{18}H_{20}O_3$	76·0	7·1	$C_{10}H_{21}$ ...	78·4	8·9	$C_{25}H_{34}O_3$	78·5	8·9
Bu	76·6	7·6	$C_{19}H_{22}O_3$	76·5	7·4	$C_{12}H_{25}$ ...	79·1	9·3	$C_{27}H_{38}O_3$	79·0	9·3
C_5H_{11} ...	76·9	7·8	$C_{20}H_{24}O_3$	76·9	7·7	$C_{16}H_{33}$ ...	79·9	9·9	$C_{31}H_{46}O_3$	79·8	9·9
C_6H_{13} ...	77·2	8·0	$C_{21}H_{26}O_3$	77·2	8·0	$C_{18}H_{37}$ ...	80·2	10·2	$C_{33}H_{50}O_3$	80·2	10·1
C_7H_{15} ...	77·7	8·2	$C_{22}H_{28}O_3$	77·6	8·3						
n-*Propyl 4'-alkoxydiphenyl-4-carboxylates.*											
Me	75·6	6·8	$C_{17}H_{18}O_3$	75·5	6·7	C_8H_{17} ...	78·3	8·7	$C_{24}H_{32}O_3$	78·3	8·7
Et	75·9	7·1	$C_{18}H_{20}O_3$	76·0	7·1	C_9H_{19} ...	78·5	8·9	$C_{25}H_{34}O_3$	78·5	9·0
Pr	76·5	7·5	$C_{19}H_{22}O_3$	76·5	7·4	$C_{10}H_{21}$ ...	78·8	9·2	$C_{26}H_{36}O_3$	78·8	9·1
Bu	76·9	7·6	$C_{20}H_{24}O_3$	76·9	7·7	$C_{12}H_{25}$ ...	79·3	9·4	$C_{28}H_{40}O_3$	79·2	9·4
C_5H_{11} ...	77·3	8·1	$C_{21}H_{26}O_3$	77·2	8·0	$C_{16}H_{33}$ ...	80·1	9·9	$C_{32}H_{48}O_3$	80·0	10·0
C_6H_{13} ...	77·5	8·3	$C_{22}H_{28}O_3$	77·6	8·3	$C_{18}H_{37}$ ...	80·3	10·2	$C_{34}H_{52}O_3$	80·3	10·3
C_7H_{15} ...	77·9	8·4	$C_{23}H_{30}O_3$	77·9	8·5						

acid. In all cases, after esterification, the mixture was a colourless solution, which was poured into an excess of aqueous sodium hydrogen carbonate. The solid was collected, washed with water, and pressed dry. The crude esters were digested with boiling ethyl alcohol, filtered hot to remove unchanged acid, and the ester crystallised from the filtrate. The solubility in ethyl alcohol is variable—in general it increases from methyl to ethyl to propyl ester—and frequently the alcoholic filtrate had to be concentrated before crystals appeared. The esters were then crystallised from light petroleum (b. p. 40—60° or 60—80° according to solubility), the solution being filtered if necessary from any remaining carboxylic acid, which is insoluble. Crystallisation was continued until the m. p.s were constant, but since the highly pure acids were used for esterification the esters were usually pure after the first crystallisation. The physical constants for the esters are recorded in Table 2.

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Organosilicon Compounds. Part XII. Substituted 9-Fluorenyltrimethylsilanes.*

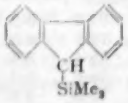
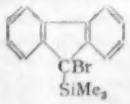
By C. Eaborn and R. A. Shaw.

[Reprint Order No. 5944.]

9-Trimethylsilylfluorene has been brominated in the 2-, 7-, and 9-position but nitration led to cleavage of the Si–C bond. The Si–C bond of 9-bromo-9-trimethylsilylfluorene was broken in reactions involving nucleophilic reagents but survived electrophilic attack on bromine. Some unusual Si–C bond cleavages are reported.

There has been little systematic study of organosilicon compounds in which the silicon is attached at a " reactive methylene " position, although they are of special interest in that the usual polarity $\overset{+}{\text{Si}}-\overset{-}{\text{C}}$ of the silicon–carbon bond is enhanced, with consequent increase in the reactivity of the bond. Sommer and Marans (*J. Amer. Chem. Soc.*, 1951, **73**, 5135) have studied trialkyl-1-indenylsilanes and we now describe the reactions of 9-trimethylsilylfluorene (I) and its derivatives.

Halogenation and Nitration.—With one equivalent of bromine in chloroform or two equivalents in carbon tetrachloride, the silane (I) gives, respectively, 2-bromo- and 2 : 7-dibromo-9-trimethylsilylfluorene. With *N*-bromosuccinimide, it gives 9-bromo-9-tri-

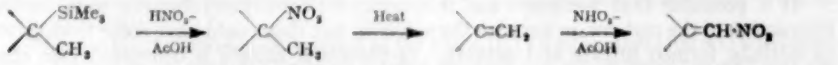
(I)   (II)

methylsilylfluorene (II), and di-9-fluorenyldimethylsilane gives di-(9-bromo-9-fluorenyl)dimethylsilane; with *N*-chlorosuccinimide the silane (I) gives 9-chloro-9-trimethylsilylfluorene.

Although nuclear bromination proceeds normally, nitration of 9-trimethylsilylfluorene in glacial acetic acid gave 2 : 9-dinitrofluorene. The cleavage of the Si–C bond probably involves electrophilic attack of a nitronium ion or a similar entity at the position 9, and this is likely to precede nuclear nitration which lowers the electron density at that position. Cleavage of a Si–C bond by electrophilic attack on an aliphatic carbon atom occurs in the interaction of β-trimethylsilylpropionic acid with sulphuric acid (Sommer, Barrie, and Gould, *ibid.*, 1953, **75**, 3765) and probably also in the interaction of tetra-alkylsilanes with iodine in presence of aluminium iodide (Eaborn, *J.*, 1949, 2755). The alternative possibility, that the cleavage results from prior replacement of the 9-hydrogen atom of (I), is unlikely because the Si–C bond of 9-methyl-9-trimethylsilylfluorene was also broken by

* Part XI, *J.*, 1955, 126.

nitration, some 9-(nitromethylene)fluorene being formed. This may have been formed by the sequence :



(Here and below represents the 9-carbon atom of fluorene.)

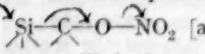
Since the Si–C cleavage in nitration involves electrophilic attack at position 9 it should be hindered by electron-withdrawing substituents on this carbon atom, and 9-bromo-9-trimethylsilylfluorene was successfully nitrated in position 2.

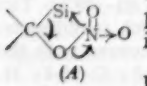
Reactions of 9-*Bromo*-9-*trimethylsilylfluorene* (II).—An α-trimethylsilyl group reduces the reactivity of alkyl halides markedly towards electrophilic reagents (Whitmore and Sommer, *J. Amer. Chem. Soc.*, **1946**, **68**, 481 ; Sommer, Bailey, Whitmore, and Strong, *ibid.*, p. 1881) for reasons which are not clear, and less so towards nucleophilic reagents (Whitmore and Sommer, *loc. cit.*), probably from a combination of polar and steric influences. While steric hindrance by an α-trimethylsilyl group will be greater in the bromo-compound (II) than in primary halides, the large difference in rate of ethanolysis between it (less than 5% of which reacts in 50 minutes at 25°) and 9-bromo-9-methylfluorene [90% of which undergoes solvolysis under the same conditions (Bartlett and Cohen, *ibid.*, **1940**, **62**, 1183)] is almost certainly because of inhibition of the S_N1 mechanism with the former compound.

No nucleophilic displacements of the bromine atom of the silane (II) occurred without cleavage of the C–Si bond. Reaction with sodium azide in aqueous methanol gave 9-azidofluorene (the nucleophile causing cleavage may not have been the azide ion, but hydroxide or alkoxide ions formed from it by solvolysis) and phenol gave 9-*p*-hydroxyphenylfluorene [which is formed from 9-bromofluorene under the same conditions (Wittig, Döser, and Lorenz, *Annalen*, **1949**, **562**, 192)]. Probably in the latter case cleavage followed replacement of the bromine since the high stability of the 9-*p*-hydroxyphenylfluorenyl carbanion should lead to very ready cleavage.

Reaction between 9-bromo-9-trimethylsilylfluorene and sodium iodide in acetone was relatively slow as judged by the rate of precipitation of sodium bromide, and fluorenone was obtained in 80% yield. The fluorenone was probably produced by decomposition of initially formed 9-iodo-9-trimethylsilylfluorene, possibly through dissociation of the latter to the 9-trimethylsilylfluorenyl free radical which absorbed oxygen to give a peroxide which then broke down to fluorenone.

Cleavage of the Si–C bond without destruction of the C–Br bond occurred when the bromo-compound (II) was heated with potassium permanganate in acetone (giving 9 : 9′-dibromo-9 : 9′-difluorenyl), and also when it was boiled with aqueous acetone (giving some 9-bromofluorene).

Primary and secondary carbonium ions with α-trimethylsilyl substituents rearrange to siliconium ions (Whitmore, Sommer, and Gold, *J. Amer. Chem. Soc.*, **1947**, **69**, 1976; Sommer, Bailey, Gould, and Whitmore, *ibid.*, 1954, **76**, 801 ; Sommer and Evans, *ibid.*, p. 1186). Rearrangement of the 9-trimethylsilylfluorenyl 9-carbonium ion is unlikely since it is stabilised by resonance and, as expected, the silane (II) was unaffected by aluminium bromide in ether. Reactions through electrophilic attack on bromine might thus be expected to lead to simple replacement of the bromine atom in this compound without Si–C bond cleavage. With silver nitrate in ethanol, the bromo-compound gave 9-ethoxy-9-trimethylsilylfluorene and some fluorenone, but only fluorenone in high yield was obtained from it by treatment with silver nitrate in aqueous acetone. Since 9-hydroxy-9-trimethylsilylfluorene was obtained without fluorenone formation on treatment with silver acetate in aqueous acetone, the fluorenone formed in the silver nitrate reaction probably came from decomposition of 9-trimethylsilyl-9-fluorenyl nitrate initially formed. The decomposition could be by either an intermolecular process, NO_3  [analogous to Baker and Easty's $E_{CO}2$ mechanism (*J.*, 1952, 1193)] or, more likely, by an intramolecular process (*A*) [the thermal



(*A*)

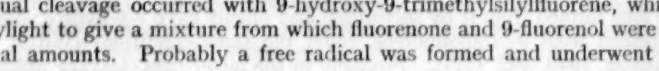
decomposition of diphenylmethyl nitrate to benzophenone (Cheeseman, *Chem. and Ind.*, 1954, 281) could have an analogous mechanism].

It is probable that 9-ethoxy- and 9-hydroxy-9-trimethylsilylfluorene were formed by interaction of the carbonium ion with the solvents, but they could have come from solvolysis of initially formed nitrate and acetate. (9-Fluorenyl nitrate is converted into ethyl 9-fluorenyl ether by ethanol.) In either case the Si–C bond seems to survive formation and reaction of the carbonium ion.

Metallation of 9-Trimethylsilylfluorene (I).—The Si–C bond also survives carbanion formation. By cross-metallation of the silane (I) (cf. Gilman, Benkeser and Dunn, *ibid.*, 1950, **72**, 1689) we have prepared the 9-lithio-derivative, and this with chloro-trimethylsilane and methyl iodide gives 9 : 9-bistrimethylsilylfluorene and 9-methyl-9-trimethylsilylfluorene, respectively.

Cleavage of the Si–C *Bond.*—Alkali readily cleaves the silane (I) but aqueous or acidic ethanol is ineffective. Cleavage is facilitated by electron-withdrawing substituents in the 9-position [see the reactions of the bromo-compound (II) above and of 9-ethoxy-9-trimethylsilylfluorene] and in the aromatic rings; 2-bromo- and 2 : 7-dibromo-9-trimethylsilylfluorene were completely cleaved even by boiling 95% aqueous ethanol in less than 18 and 1½ hours, respectively, while 9-bromo-2-nitro-9-trimethylsilylfluorene was completely cleaved by aqueous acetone in ½ hour at room temperature. 9-Ethoxy-9-trimethylsilylfluorene, which is readily cleaved by alkali, is stable to neutral aqueous ethanol but is cleaved by aqueous-ethanolic hydrochloric acid. The acidic cleavage probably involves initial attachment of a proton to the ethereal oxygen atom, to give a positively charged entity in which the silicon atom will be particularly susceptible to nucleophilic attack by the solvent.

An unusual cleavage occurred with 9-hydroxy-9-trimethylsilylfluorene, which decomposed in daylight to give a mixture from which fluorenone and 9-fluorenol were isolated in roughly equal amounts. Probably a free radical was formed and underwent disproportionation:



The 9-hydroxyfluorenyl radical has been proposed as an intermediate in the photochemical decomposition of " fluorenopinacol " in acetone to fluorenone and *iso*propyl alcohol (Schönberg and Mustafa, *J.*, 1944, 67).

Experimental

Cleavage Reactions.—Unless otherwise stated, reaction mixtures were added to water and the solid was either filtered off or taken up in ether and recovered. When the rate of cleavage was of interest samples of the mixture were withdrawn at intervals and added to water, and the m. p. (after drying) of the solid was found; this procedure is denoted below by " method A."

In " *x*% aqueous ethanol " and similar phrases, *x* denotes the vol.-% of organic solvent.

9-Trimethylsilylfluorene (I).—This, m. p. 97·5° (from ethanol), was prepared in *ca.* 60% yields by interaction of chlorotrimethylsilane with 9-fluorenyl-lithium in ether or 9-fluorenylsodium in light petroleum.

Over 95% recoveries, with no evidence of cleavage, were made when the silane was boiled with 90% aqueous ethanol for 18 hr., with 70% aqueous ethanol containing 10% of hydrochloric acid for 3 hr., and with silver nitrate (3%) in 92% aqueous acetone for 3 hr., and when its solution in glacial acetic acid was kept at room temperature for 24 hr. In ½ hr., with boiling 90% aqueous ethanol containing 10% potassium hydroxide, it gave fluorene in 94% yield.

" Method A " showed cleavage to be complete in 6 hr. when the silane was boiled with a saturated solution of sodium azide in 90% aqueous methanol, and fluorene (97%) was obtained.

Di-9-fluorenyldimethylsilane.—To 9-fluorenylsodium, prepared from sodamide (10 g.) and fluorene (56 g.) in decalin and washed with light petroleum, benzene (100 ml.) was added, followed by a solution of chlorotrimethylsilane (18 g.) in light petroleum (b. p. 40—60°). The mixture was boiled for 12 hr., and then filtered. Evaporation left an oil which solidified on addition of moist acetone. Fractional crystallization from acetone and *cyclo*hexane gave the readily soluble *di-9-fluorenyldimethylsilane*, m. p. 178—179° (1·7 g., 3%) (Found: C, 86·1; H, 6·25. $C_{28}H_{24}Si$ requires C, 86·6; H, 6·2%), and the sparingly soluble *s-di-9-fluorenyltetramethyldisiloxane*, m. p. 216—217° (0·52 g., 0·7%) (Found: C, 77·5; H, 6·4%; *M*, *ca.* 400.

$C_{30}H_{30}OSi_2$ requires C, 77·9; H, 6·5%; *M*, 450). Both products gave fluorene in ~90% yield on alkaline cleavage, the former after 1 hr. in boiling 97% aqueous ethanol containing 3% of potassium hydroxide and the latter after 3 hr. in 98% aqueous acetone containing 0·8% of potassium hydroxide.

9 : 9-*Bistrimethylsilylfluorene.*—A solution of the silane (I) (7·9 g.) in ether (100 ml.) was added to *n*-butyl-lithium [from lithium (1 g.) and *n*-butyl bromide (5·5 g.)] in ether (35 ml.) and the mixture was boiled for 3 hr. Chlorotrimethylsilane (4·5 g.) in ether (20 ml.) was added dropwise, and the mixture was set aside overnight and then filtered. The filtrate was evaporated, and the organic matter was extracted from the residue with chloroform and then recovered. Recrystallization from ethanol and acetone gave 9 : 9-*bistrimethylsilylfluorene*, m. p. 110° (1·76 g., 17%) (Found : C, 73·2; H, 8·5. $C_{19}H_{26}Si_2$ requires C, 73·5; H, 8·4%). (The remaining product had m. p. 60—90° and was probably a mixture of the initial and the final silane, since it gave pure fluorene with alcoholic alkali.)

Boiling for 24 hr. with 90% aqueous ethanol did not affect 9 : 9-bistrimethylsilylfluorene, but boiling for ¼ hr. with this solvent containing 10% of potassium hydroxide gave a 90% yield of fluorene.

9-*Methyl*-9-*trimethylsilylfluorene.*—Metallation of the silane (I) (8·7 g.) in ether with *n*-butyl-lithium was followed by addition of methyl iodide (20 g.) in ether. The mixture was boiled for 4 hr. and then worked up as in the previous experiment, but with recrystallization from ethanol, to give 9-*methyl*-9-*trimethylsilylfluorene*, m. p. 118° (2·86 g., 31%) (Found : C, 80·5; H, 7·5. $C_{17}H_{20}Si$ requires C, 80·9; H, 8·0%). This compound gave 9-methylfluorene, m. p. and mixed m. p. 45—47° in 91% yield when boiled for ¼ hr. with 90% aqueous ethanol containing 10% of potassium hydroxide.

Halogenation.—(i) A solution of bromine (1·18 g.) in chloroform (5 ml.) was added to a solution of the silane (I) (1·78 g.) in chloroform (20 ml.) during 45 min.; the mixture was boiled for 2 hr. and then decolorized with charcoal. Evaporation left a residue which was recrystallized from acetone, to give 2-*bromo*-9-*trimethylsilylfluorene*, m. p. 116·5° (0·9 g., 23%) (Found : C, 60·8; H, 5·3. $C_{16}H_{17}BrSi$ requires C, 60·6; H, 5·4%). When the product was boiled with 90% aqueous alcohol cleavage was complete in 18 hr. (method A), and 2-bromofluorene, m. p. and mixed m. p. 110·5—111·5°, was obtained in 90% yield.

Similarly, from bromine (3·5 ml.) and the silane (I) (5·15 g.) in chloroform, but with 3 hr. at 0° instead of the b. p., there was obtained 2 : 7-*dibromo*-9-*trimethylsilylfluorene*, m. p. 149° (3·93 g., 46%) (Found : C, 47·8; H, 3·9. $C_{16}H_{16}Br_2Si$ requires C, 48·5; H, 4·1%).

When the product was boiled with 90% aqueous alcohol cleavage was complete in 1½ hr. (method A) and 2 : 7-dibromofluorene, m. p. and mixed m. p. 163—164°, was obtained in 90% yield.

(ii) Boiling the silane (I) (50 g.) with *N*-bromosuccinimide (41·5 g.) in carbon tetrachloride for 11 hr. followed by filtration and concentration of the solution gave 9-*bromo*-9-*trimethylsilylfluorene* (II), m. p. 134·5° (65 g., 98%) (Found : C, 60·4; H, 5·6; Br, 25·2. $C_{16}H_{17}BrSi$ requires C, 60·6; H, 5·4; Br, 25·2%).

Similarly di-9-fluorenyldimethylsilane (0·88 g.) and *N*-bromosuccimide (1·0 g.) gave *di*-(9-*bromo*-9-*fluorenyl*)*dimethylsilane*, m. p. 220—230° (with decomp. above 200° and formation of a deep red liquid) (from ethanol) (0·45 g., 36%) (Found : C, 61·4; H, 4·3. $C_{28}H_{22}Br_2Si$ requires C, 61·5; H, 4·1%).

(iii) A mixture of *N*-chlorosuccinimide (2·3 g.), benzoyl peroxide (0·2 g.), and the silane (I) (3·8 g.) in carbon tetrachloride (20 ml.) was boiled for 3 hr., under illumination from a 150-w lamp, to give 9-*chloro*-9-*trimethylsilylfluorene*, m. p. 122° (from acetone) (1·16 g., 27%) (Found : C, 69·6; H, 6·3. $C_{16}H_{17}ClSi$ requires C, 70·4; H, 6·3%).

Nitration.—(i) Nitric acid (*d*, 1·4) (4·5 ml.) was added during 15 min. to the silane (I) (5 g.) dissolved in glacial acetic acid (42 ml.). The temperature of the mixture was raised to 80° and then allowed to fall slowly. The solid which separated was washed with acetic acid and water and recrystallized from benzene to give 2 : 9-dinitrofluorene, m. p. and mixed m. p. 136—137° (2·4 g., 41%) (Found : C, 61·0; H, 3·1; N, 11·2. Calc. for $C_{13}H_8O_4N_2$: C, 60·9; H, 3·15; N, 10·9%).

(ii) Nitration of 9-methyl-9-trimethylsilylfluorene was similarly performed, but exothermic reaction caused the temperature to rise above 100°. The mixture was poured into water, and the organic matter was extracted with ether. The solvent was removed, to leave a residue which on recrystallization from acetone gave orange-red 9-nitromethylenefluorene, m. p. and mixed m. p. 133·5—134° (Found : C, 75·3; H, 4·1; N, 6·6. Calc. for $C_{14}H_9O_2N$: C, 75·3; H, 4·1; N, 6·3%). Its ultraviolet absorption spectrum was identical with that of an authentic sample (prepared by

boiling together 9-iminofluorene and nitromethane for 3½ hr., removing the solvent, and purifying the residue by chromatography on alumina).

Its infrared spectrum had maxima at 1656, 1613, 1572, 1522, 1473, 1397, 1346, 1117, 1004, 958, 917, 852, 788, 749, and 732 cm.$^{-1}$, indicating the absence of an exocyclic methylene group which has a maximum at 890 cm.$^{-1}$.

(iii) Nitric acid (2 ml.; *d* 1·52) in acetic anhydride (10 ml.) was added slowly to a suspension of the bromo-silane (II) (6·4 g.) in acetic anhydride (25 ml.). The mixture was stirred for 2 hr. and then cooled to 0°. The precipitate was recrystallised from acetone, to give pale yellow *9-bromo-2-nitro-9-trimethylsilylfluorene*, m. p. 160° (4·06 g., 56%) (Found: C, 53·1; H, 4·1; N, 4·1. $C_{16}H_{16}O_2NBrSi$ requires C, 53·0; H, 4·45; N, 3·9%).

Cleavage by 90% aqueous acetone for 1 hr. at *ca.* 18° gave a 90% yield of 9-bromo-2-nitrofluorene, m. p. and mixed m. p. 144°. The solution contained no bromide ion.

Interaction of the Silane (II) *and Silver Salts.*—(i) A precipitate formed immediately when a boiling solution of silver nitrate (2·63 g.) in ethanol (100 ml.) was added to a boiling solution of the silane (II) (4·91 g.) in ethanol (50 ml.). The mixture was boiled for 10 min. and filtered, to give silver bromide (2·80 g., 96%). Evaporation of the filtrate left a residue which was taken up in chloroform, and the solution was filtered and evaporated. Fractional crystallization of the residue from aqueous ethanol gave *9-ethoxy-9-trimethylsilylfluorene*, m. p. 76° (from aqueous ethanol, acetone, or light petroleum) (1·46 g., 33%) (Found: C, 76·6; H, 7·7. $C_{18}H_{22}OSi$ requires C, 76·55; H, 7·9%), and fluorenone (0·23 g., 8%), m. p. and mixed m. p. 82—83°.

There was no detectable cleavage when the former product was boiled with 90% aqueous ethanol for 6 hr. Method A showed cleavage to be complete in 18 hr. in boiling 75% aqueous ethanol containing hydrochloric acid (3N), and ethyl 9-fluorenyl ether, m. p. and mixed m. p. 50—52°, was obtained in 80% yield.

Cleavage with 90% aqueous ethanol containing 10% of potassium hydroxide for ½ hr. gave ethyl 9-fluorenyl ether, m. p. and mixed m. p. 52—54°, in 82% yield and no unchanged material.

(ii) When the solution of the silane (II) (3·9 g.) in acetone (50 ml.) was added to a solution of silver nitrate (2·1 g.) in 20% aqueous acetone (25 ml.) a precipitate formed immediately and the liquid became deep yellow. After ½ hr. the silver bromide (2·28 g., 98%) was filtered off, and the solvent was removed from the filtrate at reduced pressure. The residue was recrystallized from light petroleum, to give fluorenone, m. p. and mixed m. p. 83—84° (1·88 g., 85%); the phenylhydrazone had m. p. and mixed m. p. 149—150°.

(iii) A solution of the silane (II) (7·63 g.) in boiling acetone (250 ml.) was added to one of silver acetate (4·0 g.) in boiling water. The mixture was boiled for ½ hr. and then filtered, and the filtrate added to water. Ether-extraction followed by drying (Na_2SO_4) and evaporation of the extract left a residue which recrystallized from light petroleum, to give *9-hydroxy-9-trimethylsilylfluorene*, m. p. 92° (2·08 g., 34%) (Found: C, 75·8; H, 7·5. $C_{16}H_{18}OSi$ requires C, 75·6; H, 7·1%).

The compound decomposed slowly in a corked tube in the dark. A sample exposed to daylight in an open dish quickly became yellow and moist but had a dry appearance again after a week. Chromatography on alumina gave fluorenone (0·11 g.) and 9-fluorenol (0·09 g.) and a small amount of a substance of m. p. >300°.

9-Fluorenyl Nitrate.—A solution of 9-bromofluorene (5·3 g.) in acetonitrile (55 ml.) was added to one of silver nitrate (3·7 g.) in acetonitrile (10 ml.) and after 2 hr. silver bromide was filtered off (4·0 g., 98%). The filtrate was decolorized with charcoal, the solvent was removed, and the residue recrystallized from light petroleum to give *9-fluorenyl nitrate*, m. p. 89° (3·0 g., 61%) (Found: C, 69·1; H, 4·1; N, 5·9. $C_{13}H_9O_3N$ requires C, 68·7; H, 4·0; N, 6·2%).

Reactions of the Bromo-compound (II).—(i) After 1 hr. at *ca.* 18° a solution of this compound (1·07 g.) in ethanol (75 ml.) was poured into water, and the precipitate was filtered off and dried, to give unchanged material (1·02 g., 95%), m. p. and mixed m. p. 133—134°. There was no bromide ion in the filtrate.

(ii) A solution of the bromide (II) (1·62 g.) in 95% aqueous acetone (50 ml.) was boiled for 3 hr. and then concentrated and cooled, to give unchanged material (0·99 g., 61%), m. p. and mixed m. p. 132—134°. The mother-liquor was evaporated to dryness and the residue, recrystallized from acetone and light petroleum, gave 9-bromofluorene (0·06 g., 5%), m. p. and mixed m. p. 102—103·5°.

(iii) A solution of the compound (II) (3·11 g.) in methanol (50 ml.) was boiled with excess of sodium azide (2 g.) for 1½ hr. and then added to water. The precipitated oil was taken up in ether, recovered, and dissolved in hot aqueous ethanol. The solution was quickly cooled in ice, to give 9-azidofluorene, m. p. and mixed m. p. 42—44° (1·72 g., 85%).

(iv) A solution of the compound (II) (1·84 g.) and sodium iodide (1·5 g.) in acetone (65 ml.) was stored in the dark for 3 days, during which a solid was slowly deposited and a deep iodine colour appeared. The solid was filtered off and identified as sodium bromide (0·56 g., 60%). The filtrate was diluted with ether and iodine was removed with aqueous sodium thiosulphate. Evaporation left a deep yellow solid, which was recrystallized from ether–light petroleum to give fluorenone, m. p. and mixed m. p. 82—83° (0·82 g., 79%).

(v) A mixture of phenol (7 g.) and the compound (II) (3·75 g.) was kept at 55° for 3½ hr., after which evolution of hydrogen bromide had stopped. *cyclo*Hexane (15 ml.) was added, and the solution was boiled for 5 min. and then allowed to cool. The solid which separated was recrystallised from *cyclo*hexane, to give 9-*p*-hydroxyphenylfluorene, m. p. and mixed m. p. 178—179° (2·62 g., 85%).

(vi) A mixture of potassium permanganate (0·98 g.) and the silane (II) (3·0 g.) and acetone (100 ml.) was boiled for 2 hr. then filtered. Evaporation left a residue which, recrystallised from benzene, gave 9 : 9′-dibromo-9 : 9′-difluorenyl, m. p. 243—244° (decomp. to a deep red liquid) (Found : C, 64·0; H, 3·4; Br, 32·3. Calc. for $C_{26}H_{16}Br_2$: C, 63·9; H, 3·3; Br, 32·8%). Ingold and Jessop (*J.*, 1929, 2360) report m. p. 236° (decomp.).

Spectra.—The ultraviolet absorption spectra of many compounds referred to above have been previously reported (Eaborn and Shaw, *J.*, 1954, 2027; on the log ε axes on p. 2028 of that paper 4·0, 4·4, and 4·8, should be replaced by 3·4, 4·0, and 4·6, respectively). The following additional data were obtained (values of $\lambda_{max.}$ in mμ with log ε in parentheses; * denotes inflexion) : 9-fluorenyl nitrate, 221 (4·40), 227·5 (4·48), 235 (4·46), 273·5 (4·14), 281·5* (4·07); *n*-butyldi-9-fluorenylamine, 230·5 (4·35), 262·5 (4·51), 296 (3·75), 307·5 (3·76); *s*-di-9-fluorenyltetramethyldisiloxane, 259·5 (4·50), 264·5 (4·49), 278* (4·06), 290 (4·23), 299·5 (4·37); 9-iodo-9-nitrofluorene, 244 (4·43); 9-iminofluorene, 217·5* (4·22), 245·5 (4·72), 254 (4·86), 290·5 (3·72), 297 (3·58), 309* (3·03), 354 (2·45), 373* (2·33); potassium 9-*aci*-nitrofluorene, 246 (4·70), 311 (3·72), 372 (4·20); 9-nitromethylenefluorene, 267·5 (4·53), 288 (3·91), 345 (4·03). The last two compounds were examined in 95% aqueous ethanol and the others in *n*-hexane.

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Homolytic Aromatic Substitution. Part IX. Competitive Experiments on the Arylation of Chlorobenzene and Nitrobenzene with p-Chlorophenyl Radicals.*

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Competitive experiments have been carried out on the action of *p*-chlorophenyl radicals derived from *p*-chlorobenzoyl peroxide on mixtures of nitrobenzene with chlorobenzene and benzene. The relative rate ratios derived therefrom are lower than the corresponding ratios previously obtained with phenyl radicals. This is considered to be due to the electrophilic character which is conferred on the *p*-chlorophenyl radical by the inductive effect of the chlorine atom.

IN Parts I—VIII (*J.*, 195, 2892; 1952, 2094; 1953, 44, 3412; 1954, 794, 2747, 3353; 1955, 6) the determination of the effects of substituent atoms or groups on the course of the homolytic phenylation of a number of aromatic compounds was reported. The method employed was the measurement of partial rate factors, which express the rate of substitution at the positions concerned relative to the rate of substitution at one position in unsubstituted benzene, for the various nuclear positions at which phenylation is possible. The present communication is concerned with the effect of a substituent, chlorine, in the attacking radical, on the nuclear substitution. Di-(*p*-chlorobenzoyl) peroxide was used

* Part VIII, *J.*, 1955, 6.

as the source of *p*-chlorophenyl radicals. This substance has been used for the arylation of pyridine, 2- and 4-*p*-chlorophenylpyridine being produced, by Hey and Walker (*J.*, 1948, 2213). This, and many other examples of aromatic arylation reactions with substituted radicals which have been reported, have demonstrated that substituted radicals behave similarly to phenyl radicals. Hey, Nechvatal, and Robinson (Part I, *loc. cit.*) showed that this similarity was supported in a quantitative sense when they demonstrated that the percentage of *meta*-substitution in nitrobenzene was unaffected by the introduction of bromo- and methyl substituents into the *para*-position of the substituting phenyl radical. On the other hand, De Tar and Kazimi (Amer. Chem. Soc., Abs. 122nd Meeting, 1952, 49M) have shown that the amount of *meta*-substitution in nitrobenzene is increased on using *m*- and *p*-nitrophenyl, in place of phenyl, radicals. In addition, Dannley and Sternfeld (*J. Amer. Chem. Soc.*, 1954, **76**, 4543) have shown that there was a marked decrease in the extent of attack on the side chain of benzotrichloride, and a marked increase in the amount of the *meta*-isomeride resulting from nuclear arylation of this compound when di-(*p*-chlorobenzoyl) peroxide was used in place of benzoyl peroxide. Even more marked effects in the same sense were observed when di-(*p*-nitrobenzoyl) peroxide was used as the source of radicals. Simamura and Migita (*Bull. Chem. Soc. Japan*, 1954, **27**, 228) have reported, from semi-quantitative measurements of the ratios of isomerides obtained in the reactions of *N*-nitrosoaceto-*p*-anisidide and *N*-nitrosoacetanilide with nitrobenzene, that the mixture obtained from the former reagent contains less of the *meta*-isomeride than that obtained from the latter. Up to the present no measurements of relative rates of substitution with substituted phenyl radicals have been reported, although such measurements are easier from a practical viewpoint, and yield as much information as measurements of ratios of isomerides. The determination of the rates of substitution, with *p*-chlorophenyl radicals, of nitrobenzene relative to chlorobenzene and benzene is therefore now reported.

Experimental Methods and Results

Direct Determination of $^{PhNO_2}_{PhCl}K$.—Experiments 1 and 2 were carried out with di-(*p*-chlorobenzoyl) peroxide (8 g.) in an equimolar mixture (200 ml.) of nitrobenzene and chlorobenzene. The reactions were allowed to proceed in a thermostat at 80° for 72 hr. The isolation and analysis of the mixed diphenyls were carried out by the standard procedure (Part II, *loc. cit.*). In the final distillation fore-runs were collected, consisting of mixed fractions containing the last traces of nitrobenzene (the higher-boiling solvent) and the first traces of dichlorodiphenyls. The fore-runs were analysed by the micro-Carius method, and a correction in terms of dichlorodiphenyls was applied to the composition of the diaryl fraction. A fraction taken immediately before the fore-run proved to consist entirely of nitrobenzene, showing that neither the fore-run nor the diaryl fraction was contaminated with residual chlorobenzene, and that the whole of the dichlorodiphenyls formed was contained in the diaryl fraction and the fore-run. The absence of chloronitrodiphenyls from the fore-runs is inferred from the observation that these compounds did not distil until a temperature 50° above that at which the fore-runs were collected had been reached. The high-boiling residue (0·2 g.) left after the distillation was of negligible influence. The results are given in Table 1.

Table 1.

Expt. no.	1	2
Diaryl fraction (g.) (b. p. 55—130°/0·1 mm.)	4·308	4·420
Nitrodiaryls (%)	63·01	60·27
Fore-run (g.) (b. p. 41—55°/0·1 mm.)	0·304	0·558
Chlorine in fore-run (%)	10·2	0·00
Dichlorodiphenyls in fore-run (g.)	0·098	0·000
Corr. wt. of diaryl fraction (g.)	4·406	4·420
Nitrodiaryls, corr. (%)	61·61	60·27
$^{PhNO_2}_{PhCl}K$	1·53	1·45
p-Cl·C_6H_4·CO_2H (g.)	3·72	3·73
(*p*-Cl·C_6H_4·CO_2)$_2$ accounted for (%)	84·0	85·0

Hence, $^{PhNO_2}_{PhCl}K$ = 1·49

Direct Determination of $^{PhNO_2}_{PhH}K$.—It was reported in Part II (*loc. cit.*) that the direct determination of this ratio for phenylation was rendered extremely difficult by the high volatility of diphenyl, which gave rise to considerable losses of diphenyl in the nitrobenzene fraction during

the final distillation. This difficulty does not arise in the present determination, when *p*-chlorophenyl radicals are used in place of phenyl radicals, since 4-chlorodiphenyl is considerably less volatile than diphenyl, and the necessary separation is therefore easily accomplished. A correction for the slight loss of 4-chlorodiphenyl which occurs in this way is made possible by the analysis of foreruns.

Expts. **3** and **4** were carried out with di-(*p*-chlorobenzoyl) peroxide (8 g.), which was allowed to decompose for 72 hr. in a thermosat at 80° in an equimolar mixture (200 ml.) of nitrobenzene and benzene. The isolation and analysis of the diaryl fraction were carried out by the standard procedure. Fore-runs were taken, and the necessary corrections to the composition of the diaryl fractions were made. Fractions taken immediately before the fore-runs proved to consist entirely of nitrobenzene. Once again, the small amount (0·2 g.) of high-boiling material left after the distillation was of negligible influence. The results are given in Table 2.

TABLE 2.

Expt. no.	3	4
Diaryl fraction (g.) (b. p. 55—130°/0·1 mm.)	3·543	3·705
Nitrodiaryls (%)	72·97	71·24
Fore-run (g.) (b. p. 41—55°/0·1 mm.)	4·286	3·501
Chlorine in fore-run (%)	1·69	1·30
Chlorodiphenyls in fore-run (g.)	0·364	0·234
Corr. wt. of diaryl fractions (g.)	3·907	3·939
Nitrodiaryls, corr. (%)	66·18	67·01
$^{PhNO_2}_{PhH}K$	1·50	1·55
p-Cl·C$_6$H$_4$·CO$_2$H (g.)	3·70	3·71
(*p*-Cl·C$_6$H$_4$·CO$_2$)$_2$ accounted for (%)	82·0	82·5
Hence, $^{PhNO_2}_{PhH}K$ =	1·53	

Preparation of Reagents.—Benzene, chlorobenzene, and nitrobenzene were purified according to the procedures described in Part II (*loc. cit.*). Di-(*p*-chlorobenzoyl) peroxide was prepared from *p*-chlorobenzoyl chloride by Hey and Walker's method (*loc. cit.*). The product was purified by recrystallisation to constant m. p. [138° (decomp.)] from chloroform–methanol.

DISCUSSION

The results of the above experiments on homolytic *p*-chlorophenylation, in comparison with the corresponding figures for phenylation (Part II, *loc. cit.*), are :

	$^{PhNO_2}_{PhCl}K$	$^{PhNO_2}_{PhH}K$		$^{PhNO_2}_{PhCl}K$	$^{PhNO_2}_{PhH}K$
Phenylation	2·78	4·0	Decrease (%)	46·0	61·5
p-Chlorophenylation	1·49	1·53			

It is apparent that the relative rate ratios in both cases have decreased significantly on replacement of the phenyl by the *p*-chlorophenyl radical, the decrease being greater in the nitrobenzene–benzene competitive experiments. In order to interpret this result it is necessary to consider the corresponding rate ratios for electrophilic substitution. Although $^{PhNO_2}_{PhH}K$ has not been determined directly for nitration, it has been established that the rate ratio is very small compared with $^{PhNO_2}_{PhCl}K$ and, further, that both ratios are very much less than unity. On the other hand, these relative rate ratios for phenylation are somewhat greater than unity, and are more nearly equal.

The results of the experiments with *p*-chlorophenyl radicals suggest that the inductive ($-I$) effect of the chlorine atom results in the withdrawal of electrons from the ring, thus reducing the probability of localisation of a single electron at the *para*-position in the radical. The *p*-chlorophenyl radical thus assumes some measure of electrophilic character. The extent to which this process takes place is uncertain, but it is predictable that a comparison of the phenyl radical with the *p*-chlorophenyl radical should reveal differences in behaviour derived from such an effect. This is the explanation of the decrease in the rate ratios for *p*-chlorophenylation when compared with phenylation. Moreover, a greater decrease would be expected in the value of $^{PhNO_2}_{PhH}K$ than in that of $^{PhNO_2}_{PhCl}K$ on using a *p*-chlorophenyl radical in place of a phenyl radical, since, for electrophilic substitution (nitration), $^{PhNO_2}_{PhCl}K$ is much greater than $^{PhNO_2}_{PhH}K$, nitrobenzene being deactivated to a

very much greater extent than chlorobenzene. The experimental observations are in accord with this requirement. Polar effects of a similar nature have been observed by Kooyman, van Helden, and Bickel (*Proc. k. ned. Akad. Wetenschap.*, 1953, *B*, **56**, 75) on the rate of removal of hydrogen atoms from the methyl group of substituted toluenes by the strongly electronegative radicals $Br^{\cdot}$ and $(CH_2{\cdot}CO)_2N^{\cdot}$, and by van Helden and Kooyman (*Rec. Trav. chim.*, 1954, **73**, 269) on the atomic chlorination of substituted toluenes and some aliphatic compounds.

These conclusions, if correct, therefore adumbrate the concept of a whole series of free radical reagents of varying electrophilic or nucleophilic character, since the presence of an electron-repelling group in a phenyl radical should confer a measure of nucleophilic character on the radical. The phenyl radical itself is regarded as unique in being the only reagent for aromatic substitution so far investigated in which polar influences are absent, since there is no reason to postulate any polarisation of this radical. The polar influences of the directing groups do not therefore play a part in determining the course of reaction, which is governed only by the factors discussed in previous papers of this series, and by Hey and Williams (*Discuss. Faraday Soc.*, 1953, **14**, 216).

In addition to the alteration of relative rates of substitution, the assumption of electrophilic or nucleophilic character on the part of the substituting radical would be expected to give rise to the formation of different proportions of the *ortho*-, *meta*-, and *para*-isomerides from those which are formed in the phenylation reaction. Such an effect has been reported by Dannley and Sternfeld (*loc. cit.*) in the *p*-chlorophenylation of benzotrichloride, and interpreted by these workers in a manner similar to that which we have outlined. Further work on these lines with *p*-chlorophenyl and other substituted radicals is now in progress.

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Acacia karroo *Gum.*

By A. J. CHARLSON, J. R. NUNN, and A. M. STEPHEN.

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Acid hydrolysis of *Acacia karroo* gum furnishes L-rhamnose (2%), L-arabinose (36%), D-galactose (50%), and D-glucuronic acid (12%). 3-*O*-β-L-Arabopyranosyl-L-arabopyranose, 4-*O*-α-D-glucuronosyl-D-galactose, and 6-*O*-β-D-glucuronosyl-D-galactose have been isolated from the products of partial hydrolysis. The gum differs markedly in structure from other *Acacia* gums so far examined.

THE compositions of the gums from *Acacia senegal* (Butler and Cretcher, *J. Amer. Chem. Soc.*, 1929, **51**, 1519), *A. mollissima* (Stephen, *J.*, 1951, 646), *A. pycnantha* (Hirst and Perlin, *J.*, 1954, 2622), and *A. cyanophylla* (Charlson, Nunn, and Stephen, *J.*, 1955, 269) differ in certain respects, though the monosaccharides and the aldobiuronic acid produced on acid hydrolysis are the same for them all. Thus, the equivalent weights and specific rotations of the gums vary from species to species, and the disaccharides isolated after graded hydrolysis differ. The gum of *A. karroo* Hayne. ("doringboom"; Karroo thorn; mimosa), a tree indigenous to South Africa and found extensively in the semi-arid inland regions, has been investigated in order to compare its composition with those of other *Acacia* gums, particularly "gum arabic" types such as *A. senegal* gum.

The equivalent weight (*ca.* 1660) of the gum acid from *A. karroo* is similar to that of the gum acid from *A. mollissima*, but by contrast the specific rotation (+54°) differs in sign from that of any other *Acacia* gum. Autohydrolysis of the gum acid produced a degraded polysaccharide acid of equivalent weight 1270, a mixture of acid oligosaccharides, L-rhamnose, L-arabinose, D-galactose, and two neutral reducing disaccharides. One of these, which was produced in low concentration and was not isolated, moved at the same rate on

paper chromatograms as the galactose-arabinose disaccharide obtained from *A. cyanophylla* and certain varieties of gum arabic (cf. Charlson, Nunn, and Stephen, *loc. cit.*). The other consisted of arabinose units only, and its optical rotation (+208°) and m. p. of the derived phenylosazone (230°) indicated that it was 3-*O*-β-L-arabopyranosyl-L-arabopyranose, obtained previously by Jones (*J.*, 1953, 1672) from larch ε-galactan and by Andrews, Ball, and Jones (*J.*, 1953, 4090) from peach gum and cherry gum. This disaccharide could not be detected amongst the hydrolysis products of *A. cyanophylla* gum, which is understandable in view of the low arabinose content of this gum, and is present apparently in traces amongst the hydrolysis products of *A. mollissima* gum (unpublished work) and "gum arabic, Turc. variety" (Jones, *loc. cit.*).

Hydrolysis of *A. karroo* gum with 0·5N-sulphuric acid gave, in addition to the monosaccharides noted above, a mixture of two aldobiuronic acids in similar amounts. Separation of the acids by partition chromatography on cellulose yielded the expected 6-*O*-β-D-glucuronosyl-D-galactose and a faster-moving acid identified as 4-*O*-α-D-glucuronosyl-D-galactose (α-configuration is indicated by the high specific rotation of both the barium salt of the acid and the fully methylated derivative; cf. A. J. Charlson, Ph.D. Thesis, Cape Town, 1954). The latter substance has been isolated from grape-fruit and lemon gums (Connell, Hainsworth, Hirst, and Jones, *J.*, 1950, 1696). Mixtures of aldobiuronic acids, indicating variety in the mode of linkage of uronic acid to the next monosaccharide unit in a gum, are present in the hydrolysis products of mesquite gum (Cunneen and Smith, *ibid.*, 1948, 1141), lemon gum (Andrews and Jones, *ibid.*, 1954, 1724), and gum myrrh (unpublished work); the mixtures from mesquite gum (Smith, *ibid.*, 1951, 2646) and gum myrrh comprise the 4-*O*-methyl-D-glucuronic acid analogues of the aldobiuronic acids obtained from *A. karroo* gum. White (*J. Amer. Chem. Soc.*, 1954, **76**, 4906) has discussed the structure of sapote gum in the light of his finding that two alkylated aldobiuronates appear among the methanolysis products of the methylated gum.

The tendency of *A. karroo* gum to become insoluble in water when dried and stored has precluded its being examined electrophoretically. The production of two aldobiuronic acids suggests that two different polysaccharides may be present in the gum, and in any event it is purposeless to attempt to express the structure of the gum in terms of a repeating unit containing a single uronic acid unit; the very low rhamnose content (as in *A. pycnantha* gum) further emphasises this. However, expressed as approximate percentages, the quantities of sugars and uronic acid produced on hydrolysis were L-rhamnose (2), L-arabinose (36), D-galactose (50), and D-glucuronic acid (12).

Experimental

Unless otherwise stated, concentration of solutions was carried out at 40°/20 mm., and specific rotations were measured in aqueous solution. Paper chromatograms were run at 27° in butanol–ethanol–water (20 : 1 : 3), ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4) (Jones, *loc. cit.*), or butanol–pyridine–water (9 : 2 : 2).

A. karroo *Gum.*—Crude gum, in the form of nearly colourless, transparent lumps, was collected near Alice in the Eastern Cape Province during autumn, through the courtesy of Mr. H. J. D. Matthews. The gum was converted into the gum acid by the procedure used in the purification of *A. cyanophylla* gum (Charlson, Nunn, and Stephen, *loc. cit.*), yielding a white amorphous powder, $[\alpha]_D$ +54° (*c*, 1·33, as sodium salt) [Found: Sulphated ash, 0·56%; equiv., 1660 (on material dried at 100°/20 mm.)].

Quantitative Hydrolysis.—*A. karroo* gum acid was hydrolysed by 1·5N-sulphuric acid for 15 hr. at 100°, and the products were separated by paper chromatography and analysed by Somogyi's method (*J. Biol. Chem.*, 1952, **195**, 19). Galactose and arabinose were found in the molar ratio 1·2 : 1; rhamnose was present, but in amount too small to estimate with accuracy.

Autohydrolysis.—The gum acid (45 g.) in water (1 l.) was heated on a boiling-water bath for 75 hr., samples being withdrawn and examined qualitatively on a paper chromatogram. Arabinose was detected after 2 hr. and two disaccharides at 3·5 hr.; the slower-moving of these moved at the same rate as the galactose-arabinose disaccharide from *A. cyanophylla* gum, and its intensity did not increase as hydrolysis proceeded. The faster-moving disaccharide increased

in amount with time. Rhamnose appeared after 12 hr. and both galactose and aldobiuronic acid after 17 hr.

A degraded acid (19 g.) was precipitated by pouring the concentrated hydrolysate into ethanol (Found, on material dried at 100°/20 mm.: Equiv., 1270). Hydrolysis of this indicated the presence of galactose and uronic acid units. A mixture of barium salts (4 g.) of low molecular weight and a sugar syrup (24 g.) were recovered from the filtrate.

The sugar syrup was fractionated on cellulose, half-saturated aqueous butanol being used, yielding α-L-rhamnose hydrate (0·9 g.), L-arabinose (15·2 g.), and D-galactose (2·0 g.), which were identified in the usual way, together with a hygroscopic disaccharide (1·6 g.). Elution with water gave a mixture of barium salts (3 g.) of low molecular weight.

Identification of Disaccharide.—This reducing compound had $[\alpha]_D^{18}$ +208° (*c*, 1·7), R_{gal} 0·58 (relative to galactose) in the basic solvent, and R_{gal} 0·72 in the acid solvent, and on hydrolysis of a portion (0·1 g.) in 0·5N-sulphuric acid for 2 hr. at 100°, arabinose only was produced (detected on a paper chromatogram).

The disaccharide formed a phenylosazone, m. p. 230° (decomp.) after recrystallisation from ethanol (Found: C, 56·6; H, 6·4; N, 12·6. Calc. for $C_{23}H_{28}O_7N_4$: C, 57·4; H, 6·1; N, 12·2%). Jones (*loc. cit.*) reports 3-*O*-β-L-arabopyranosyl-L-arabinose as having $[\alpha]_D$ +220° ±10°, R_{gal} 0·69 (basic solvent), 0·79 (acid solvent); osazone, m. p. 235°. The disaccharide crystallised during several months. Methylation of the disaccharide (1·0 g.) afforded a syrup (1·1 g.) having n_D^{20} 1·469, $[\alpha]_D^{20}$ +230° (*c*, 0·79); a portion (0·1 g.) was distilled, the syrup (0·07 g.) having b. p. 130—150°/4 × 10^{-3} mm. (Found: OMe, 50·3. Calc. for $C_{16}H_{30}O_9$: 6OMe, 50·6%).

Hydrolysis of the methylated product (0·5 g.) yielded a syrup (0·48 g.) which exhibited two spots, R_{MG} 0·92 (relative to tetramethylgalactose) and R_{MG} 0·78, and a much fainter spot, R_{MG} 0·60 (basic solvent). Fractionation on cellulose gave: (i) a syrup (0·19 g.), $[\alpha]_D^{19}$ +145° (*c*, 1·1), R_{MG} 0·92, which on bromine oxidation and treatment with phenylhydrazine afforded 2 : 3 : 4-tri-*O*-methyl-L-arabonophenylhydrazide, m. p. 153—155° (lit., m. p. 156°, 158°, 160°); (ii) a mixture of methylated sugars (0·12 g.); and (iii) a di-*O*-methylarabinose (0·11 g.), $[\alpha]_D^{22}$ +120° (*c*, 0·94), R_{MG} 0·78. From this was prepared an *N*-phenyl-L-arabinosylamine dimethyl ether, m. p. 136—137° after recrystallisation from butanol, unchanged on admixture with the 2 : 4-dimethyl ether described by Charlson, Nunn, and Stephen (*loc. cit.*).

Aldobiuronic Acids.—A mixture of *A. karroo* gum acid (40 g.) and 0·5N-sulphuric acid (300 c.c.) was heated for 15 hr. at 95°, then cooled, neutralised with barium carbonate, and filtered. A barium salt (10 g.), $[\alpha_D^{20}]$ +70°, was precipitated when the concentrated filtrate was poured into methanol (2 l.) (Found: Ba, 13·9%). Examination of the salt on a paper chromatogram (acid solvent; 72 hr.) revealed the presence of a hexuronic acid, two aldobiuronic acids (R_{gal} 0·34 and 0·27), and smaller amounts of oligosaccharide. The mixture, after removal of barium, was separated on cellulose, butanol–water–formic acid (45 : 4 : 1) being used. This afforded acid (I) (1·6 g.), R_{gal} 0·34 {barium salt, $[\alpha]_D^{21}$ +110° (*c*, 2·1) (Found: Ba, 15·3%)}; then a mixture (1·0 g.) of the two acids; and next acid (II) (0·6 g.), R_{gal} 0·27 {barium salt, $[\alpha]_D^{23}$ +12° (*c*, 2·0)}. A larger-scale chromatogram (with 23 g. of mixed acids) yielded 8·3 g. of acid (I) as barium salt (Found: Ba, 16·4%).

Hydrolysis of acid (I) in 2N-sulphuric acid for 15 hr. at 100° gave galactose, glucuronic acid, and glucurone. Galactose was shown to be the aglycone portion of the molecule by treatment of the barium salt with bromine water (Hudson and Isbell, *Bur. Stand. J. Res.*, 1929, **3**, 58); the galactose moiety was thereby oxidized. The aldobiuronic acid (2·5 g.) was then methylated with dimethyl sulphate and sodium hydroxide, followed by treatment with Purdie's reagents; distillation of the product afforded a syrup (0·9 g.), $[\alpha]_D^{18}$ +94° (*c*, 1·5 in MeOH). This material was hydrolysed in a sealed tube at 100° for 20 hr. with 2N-sulphuric acid; the solution was neutralised ($BaCO_3$), filtered, and evaporated nearly to dryness. The residue was extracted with chloroform, which was evaporated after being dried (Na_2SO_4) to give a pale yellow syrup (0·3 g.), $[\alpha]_D^{20}$ +92° (*c*, 2·27), R_{MG} 0·88 (acid bath) and 0·83 (basic bath). The syrup (0·2 g.) was oxidised with bromine water (4·5 days), and, after removal of bromine by aeration, the solution was neutralised with silver carbonate and filtered, and silver ion precipitated with hydrogen sulphide. The filtrate from this treatment was evaporated to dryness *in vacuo*, and the residue extracted with dry ether; colourless needles, m. p. 98°, were obtained on concentration of the extract (Found: C, 49·1; H, 7·4%; equiv., 240. Calc. for $C_5H_{10}O_6$: C, 49·1; H, 7·3%; equiv., 220); $[\alpha]_D$ −20° (*c*, 0·7; final value). An *X*-ray powder diagram was identical with that of authentic 2 : 3 : 6-tri-*O*-methyl-D-galactono-γ-lactone. Taken in conjunction with the hydrolytic (cf. Cunneen and Smith, *loc. cit.*). and rotational evidence, this indicates that aldobiuronic acid (I) is 4-*O*-α-D-glucuronosyl-D-galactopyranose.

Acid (II) was methylated to a crystalline derivative, m. p. 89°, $[\alpha]_D^{22}$ −30° (*c*, 0·9 in $CHCl_3$), identical (mixed m. p.) with the hepta-*O*-methyl methyl ester of 6-*O*-β-D-glucuronosyl-D-galactose obtained from *A. cyanophylla* gum (Charlson, Nunn, and Stephen, *loc. cit.*).

The authors thank Dr. W. Schaffer for *X*-ray analyses and Professor J. K. N. Jones for a specimen of 2 : 3 : 6-tri-*O*-methyl-D-galactono-γ-lactone. One of them (A. J. C.) thanks African Explosives and Chemical Industries Ltd. for a research grant, and another (J. R. N.) is indebted to the South African Council for Scientific and Industrial Research for permission to participate in this work.

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The Degradation of Carbohydrates by Alkali. Part IX. Cellobiose, Cellobiulose, Cellotetraose, and Laminarin.*

By W. M. CORBETT and J. KENNER.

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Cellobiose and cellobiulose suffer degradation by alkali corresponding to that recorded in other instances (*J.*, 1953, 2245; 1954, 1789). Cellotetraose and laminarin undergo peeling processes which are regarded as illustrative of the course of alkaline degradation of hydro- and oxy-celluloses.

THIS series of papers originated from consideration of the behaviour of carbonyl oxycelluloses towards alkali. It was thus necessary to extend our previous studies of disaccharides from this standpoint to the case of cellobiose and of cellobiulose, after preparing the latter from cellobiose by the usual procedure with lime-water. The course of the degradation in each case to D-gluco*iso*saccharinic acids and D-glucose conformed to expectation, the rates of reaction approximating closely to those of lactose (Corbett and Kenner, *J.*, 1953, 2245) and lactulose (*idem*, *J.*, 1954, 1789) respectively, and is to be similarly formulated.

Cellobiose is the ultimate member, apart from glucose itself, of the series of hydrocelluloses. These result from the acidic degradation of cellulose, and so are liable to arise during its separation from the other constituents of wood by the sulphite method. Murumow, Sack, and Tollens (*Ber.*, 1901, **34**, 1427), having prepared such a product by the action of sulphuric acid on cellulose, converted it by treatment with calcium hydroxide

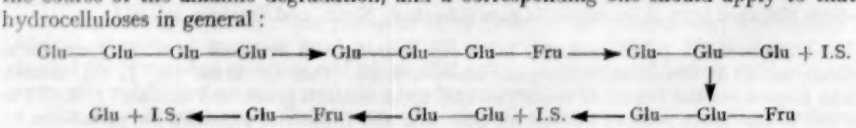
TABLE 1. *Degradation of cellotetraose by lime-water at 25°.*

Time (hr.)	Glucose units decompd. (10^{-5} mole) (1 ml. sample)	Decompn. (%)	Acids produced (eq./mole) (back-titration resin method)		Initial detection of components by paper chromatography
7	0·230	4·7	0·135	0·155	
24	1·037	21·0	0·910	0·880	Cellotriose, cellotriulose, cellobiose, cellobiulose
48	1·912	38·8	1·865	1·680	Glucose
72	2·282	46·3	2·530	2·045	Fructose
168	2·719	55·2	3·520	3·045	
192	2·984	60·5	3·645	2·975	
216	3·007	61·0	3·685	2·960	

into a mixture of essentially D-*iso*saccharinic acids with what was regarded as unchanged cellulose, but it is obviously desirable to supplement this broad picture of the alkaline degradation of mixed hydrocelluloses by a kinetic study in the case of a definite entity belonging to this group of compounds. Table 1 summarises the observations made on a solution in oxygen-free lime-water (25 ml.; 0·0397N) at 25° of cellotetraose (0·2048 g.).

* Part VIII, *J.*, 1954, 3281.

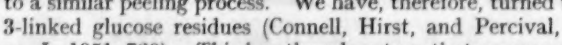
According to the ideas developed in this series, the following scheme should represent the course of the alkaline degradation, and a corresponding one should apply to that of hydrocelluloses in general:



(Glu = Glucose residue; Fru = fructose residue; I.S. = glucoisosaccharinic acid)

The relative reactivities of the tetraose, triose, and biose are likely to be approximately equal, and it is therefore not surprising that some glucose arises after decomposition has attained only at most *ca.* 40%.

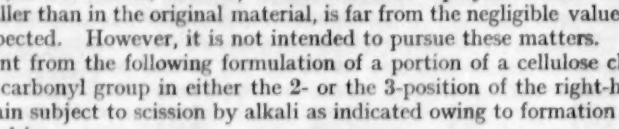
Unfortunately individual macrohydrocelluloses are not at present accessible. The products examined by Tollens and his collaborators were certainly mixtures and, as they stated, contaminated with unchanged cellulose (cf. Schwalbe and Becker, *J. pr. chem.*, 1920, **100**, 19). However, other oligosaccharides with a free carbonyl group and a 1 : 4-, a 1 : 3-, or, less directly (cf. Corbett and Kenner, *J.*, 1954, 3281), a 1 : 6-chain structure should be liable to a similar peeling process. We have, therefore, turned to laminarin with its chain of 1 : 3-linked glucose residues (Connell, Hirst, and Percival, *J.*, 1950, **3494**; Percival and Ross, *J.*, 1951, 720). This has the advantage that no rearrangements should be requisite between successive stages of the peeling process, formulated as follows:



(M.S. = D-Glucometasaccharinic acid) (n = *ca.* 40)

In fact, this reaction constitutes a most convenient source of D-glucometasaccharinic acids (B.P. Appln. 21,242/1953) and the general course of the degradation of "insoluble" laminarin was such that, in accordance with this equation, the rate of formation of D-glucometasaccharinic acids corresponded to that of laminarin degradation expressed in terms of glucose equivalents, though the reaction ceased when the degree of degradation amounted to about 48%. This was due to some inhibitive variation in chain structure because reactivity of the residue towards alkali was revived by partial hydrolysis with oxalic acid. As to the nature of the variation, Peat, Whelan, and Lawley (*Biochem. J.*, 1954, **54**, xxxiii) detected gentiobiose and ββ-trehalose among the products of acid hydrolysis of "insoluble" laminarin. The former is indicative of 1 : 6-branching and it is obvious that if the action of alkali should generate a metasaccharinic acid carrying in the 6-position a chain of hexose residues these would not be subject to further degradation. On the other hand a 1 : 1-trehalose linking is irreconcilable with a chain system of 1 : 3-linkages carrying a free aldehydic group at one end as required by our experiments, and so must be part of a separate system. Some indication of such heterogeneity of the laminarin was supported by chromatographic evidence of the transient appearance of glucose and fructose among the products of alkaline degradation—they should only arise when the end of a 1 : 3-chain system is reached. The result of hypoiodite estimation of aldehyde groups (compare Connell, Hirst, and Percival, *loc. cit.*) in our unreactive polysaccharide residues, whilst definitely smaller than in the original material, is far from the negligible value which might have been expected. However, it is not intended to pursue these matters.

It is evident from the following formulation of a portion of a cellulose chain that the presence of a carbonyl group in either the 2- or the 3-position of the right-hand ring will render the chain subject to scission by alkali as indicated owing to formation of a common doubly charged ion:



The left-hand scission product would constitute the anion of a hydrocellulose liable to peeling and, as indicated by the Head's results previously cited (Corbett and Kenner, *J.*, 1953, 2245), should also arise if the carbonyl group is in position 6. The connection

between oxy- and hydro-celluloses detected by Tollens (*Ber.*, 1901, **34**, 1434) is thus explained and is technically important in the viscose process and in the " tendering " of cellulose by oxidation.

Corbett and Kenner (*J.*, 1954, 1789) mentioned that the acids produced during the degradation of lactulose could not be satisfactorily determined by observing the decrease in alkalinity of the solution. With cellobiose, cellobiulose, and cellotetraose we experienced similar difficulty, as illustrated in the Table 1 and have found that it is not due to monosaccharides or to saccharinic acids produced during the degradation. Since it is possible to estimate reasonably accurately the acids produced by removal of all cations by ion-exchange resin, and then titrating the acids thus produced, the apparent excess of acid found by the usual method seems to arise from absorption of calcium hydroxide by the 1 : 4-linked glucosans. No such absorption has been detected in any other type of glucosan and the comparative stability of complexes towards acids indicates that they differ in nature from those occurring in the familiar sucrose–lime case.

Experimental

Cellobiose.—A solution (100 ml.) of chromatographically pure cellobiose (0·8636 g.) in oxygen-free lime-water (0·0425N) was kept at 25°. Aliquot portions were withdrawn periodically and run into excess of washed (3 × 25 ml.) Amberlite IR-120(H) resin (2·3 g.). After filtration and washing of the resin with water (3 × 10 ml.) the solution was titrated against 0·01N-sodium hydroxide (phenolphthalein). This procedure was adopted in preference to treatment of the aliquot sample with sulphuric acid and back-titration after a certain period because the latter, as the following instance illustrates, furnished unexplained higher results: (*a*) back-titration after (1) ½ hr., 1·318 acid equivs.; (2) ½ hr., 1·315; (3) 1 hr., 1·311; (*b*) resin treatment, 1·185. Mono- and di-saccharides were determined by Corbett's method (*Chem. and Ind.*, 1953, 1285). On this basis, Table 2 summarises the observations.

Table 2. *Degradation of cellobiose by lime-water at 25°.*

Time (hr.)	Cellobiose decompd. (%)	Monoses produced (moles/mole)	Saccharinic acids produced [1] (equiv./mole)	Total acids produced (equiv./mole)	Substances found by paper chromatography [2]
1	0·8	0·006	—	0·038	Cellobiulose
2	1·1	0·006	—	0·058	
3	1·9	0·022	—	0·054	Cellobiulose
4	4·6	0·050	—	0·054	
5	5·0	0·061	—	0·086	Glucose
6	6·6	0·083	—	0·123	
7	7·5	0·087		0·123	
24	39·0	0·441	0·380	0·478	Fructose
30	49·5	0·540	0·400	0·595	
48	69·7	0·707	0·631	0·840	
54	72·0	0·702	0·660	0·898	
72	79·7	0·752	0·800	1·038	Cellobiose and cellobiulose (very faint)
79	83·5	0·772	0·785	1·080	
144	90·2	0·756	1·030	1·305	No disaccharide

[1] Cf. Kenner and Richards, *J.*, 1954, 1784. [2] Ketoses detected by naptharesorcinol spray, aldoses and ketoses by silver nitrate spray. Salient features only of the chromatographic observations are noted.

Cellobiulose.—Application to cellobiose of the procedure detailed for lactulose (Corbett and Kenner, *J.*, 1954, 1789) yielded a white highly hygroscopic amorphous *ketose*, $[\alpha]_D^{23}$ (equil.) −60·1° (*c*, 2·40 in H_2O), reducing power (ferricyanide) 1·40 (glucose 1·00) (Found: C, 41·7; H, 7·0. $C_{12}H_{22}O_{11}$ requires C, 42·1; H, 6·5%).

Table 3 summarises observations made on a solution (50 ml.) of 0·4767 g. in oxygen-free lime-water (0·0424N) at 25°. In consequence of the formation of glucose and its gradual degradation to lactic acid from the outset of this experiment, the proportion of alkali used proved insufficient for completion of the degradation, but the results conform to expectation and suffice to demonstrate the nature of the reaction involved.

Cellotetraose.—A solution (25 ml.) of cellotetraose [0·2048 g.; $[\alpha]_D^{20}$ +11·6° (*c*, 1·21 in H_2O);

D.P. 4·18 by hypoiodite], kindly supplied by Dr. D. I. MacGilvray of this Association, in oxygen-free lime-water (0·0397N) was kept at 25°. Duplicate samples (1 ml. each) were withdrawn periodically, one being run on to excess of washed Amberlite IR-120(H) resin and filtered, and the combined filtrate and washings (3 × 10 ml.) titrated against 0·01N-sodium hydroxide (phenolphthalein). The other sample was run into 0·01N-sulphuric acid (5 ml.) and titrated after 15 min. against 0·01N-sodium hydroxide; this solution, acidified with N-sulphuric acid

TABLE 3.* *Degradation of cellobiulose by lime-water at 25°.*

Time (hr.)	Cellobiulose decompd. (%)	Monoses produced (moles/mole)	Saccharinic acids produced (equiv./mole)	Total acids produced (equiv./mole)	Substances found by paper chromatography
1	8·2	0·113	0·125	0·110	Cellobiose, glucose
3	19·1	0·206	0·187	0·242	
5	26·2	0·282	0·258	0·298	
24	65·5	0·565	0·555	0·659	Fructose
48	75·4	0·690	0·660	0·998	
72	76·8	0·594	0·707	Not determined	
144	80·8	0·588	0·746	1·113	

* See notes to Table 2.

(10 ml.), was then heated for 4 hr. under reflux on a boiling-water bath, cooled, exactly neutralised with 0·5N-sodium hydroxide, and diluted to 50 ml.; the glucose content of this solution was estimated, in 2-ml. samples, by the standard Hagedorn–Jensen method (*Biochem. Z.*, **1923**, **135**, 46). Preliminary experiments with both cellotetraose and cellobiose had confirmed the efficacy of this procedure, although in the former case it was necessary to multiply the experimentally determined value by a factor of 1·15. As will be seen from Table 1 the degree of degradation was stable at about 60%, although the solution was alkaline. This may be due to formation of an alkali-resistant complex between residual carbohydrate and calcium hydroxide.

Laminarin.—Samples of " insoluble " and " soluble " material were kindly supplied by the Director of the Institute of Seaweed Research.

A solution of " insoluble " laminarin (Sample No. I.L.7) (50 g.) in an oxygen-free aqueous suspension (1 l.) of calcium hydroxide (50 g.) which had been kept for 8 days at 25° was filtered and treated with the required amount of oxalic acid to remove calcium ions. Concentration of the solution to 500 ml. under reduced pressure at 50° caused separation of polysaccharide (21·4 g.). Evaporation of the filtrate and aqueous washings under reduced pressure at 50° yielded a syrup, successive extractions of which by alcohol (3 × 100 ml.) left further polysaccharide (7·7 g.). The syrup of α- and β-metasaccharins (13·8 g.), remaining after evaporation of the alcoholic extracts at 45°, furnished calcium salts (13·1 g.) from which, when their solution in hot water (31 ml.) was cooled, calcium β-metasaccharinate (5·7 g.) separated as cubic crystals, $[\alpha]_D^{20}$ −23·4° (*c*, 2·05 in H_2O) {Nef, *Annalen*, 1910, **376**, 95, gave $[\alpha]_D^{20}$ −23·25° (*c*, 4 in H_2O)}; β-metasaccharinolactone, m. p. 87—91° from ethyl acetate $[\alpha]_D^{21}$ +8·27° (*c*, 1·21 in H_2O) (Found: C, 44·1; H, 6·2. Calc. for $C_6H_{10}O_5$: C, 44·4; H, 6·2%), was obtained quantitatively from it (Nef, *loc. cit.*, gave m. p. 92°, $[\alpha]_D^{20}$ +8·2° in H_2O). Gradual addition of alcohol to the mother-liquors caused separation of solid as follows: (1) 0·13 g., $[\alpha]_D^{20}$ −23·4° (*c*, 1·97 in H_2O), from 45% ethanol; (2) 3·13 g., $[\alpha]_D^{21}$ −9·5° (*c*, 2·00 in H_2O), from 54% ethanol; (3) calcium α-metasaccharinate (0·60 g.), $[\alpha]_D^{21}$ −5·0 (*c*, 1·99 in H_2O), from 64% ethanol (Kenner and Richards, *J.*, **1954**, 278, found $[\alpha]_D^{21}$ −5·2°); (4) 0·13 g., $[\alpha]_D^{20}$ −8·7° (*c*, 2·07 in H_2O), from 74% ethanol; (5) 0·11 g., $[\alpha]_D^{21}$ −12·3° (*c*, 0·81 in H_2O), on evaporation of the mother-liquors and digestion of the residue with ethanol. Evaporation of the alcoholic liquors yielded 0·27 g., $[\alpha]_D^{22}$ −7·4° (*c*, 2·16 in H_2O). After a solution of polysaccharide (50 g.) (recovered as above) in N-oxalic acid (1·5 l.) had been heated at 100° for 2 hr., excess of calcium hydroxide was added and heating continued for 2½ hr. in a stream of nitrogen. Treatment of the product as above yielded polysaccharide (10·9 g.), calcium β-metasaccharinate (7·9 g.), $[\alpha]_D^{23}$ −22·1° (*c*, 2·0 in H_2O), and crude calcium α-metasaccharinate (11·6 g.), $[\alpha]_D^{23}$ −6·1° (*c*, 2·0 in H_2O).

The following Table records the behaviour at 25° under oxygen-free conditions of a solution of " insoluble " laminarin (No. I.L 4) (0·5750 g.) in warm water (5 ml.) diluted with lime-water to 100 ml. (final normality 0·0398). The acids were determined by back-titration; the glucose produced by hydrolysis of a sample (10 ml.; initially 0·165 mg. of laminarin) with 4N-sulphuric acid (5 ml.) for 1 hr. at 100° was estimated by the Hagedorn–Jensen method. Glucose and fructose were detected after 72 hr., but their concentrations appeared to diminish after 7 days.

Time (hr.)	0·125	1	2	6	23	47
Equiv. of acids produced per glucose unit	0·000	0·014	0·023	0·086	0·240	0·321
Glucose units decompd. (%)	0·0	*	*	11·0	30·6	37·7
Time (hr.)	71	143	215	240	311	
Equiv. of acids produced per glucose unit	0·350	0·386	0·417	0·434	0·424	
Glucose units decompd. (%)	*	*	*	48·5	47·7	

* Not determined.

Similarly, a solution of " soluble " laminarin (50 g.) in an oxygen-free aqueous suspension (1 l.) of calcium hydroxide (50 g.) at 100° furnished after 3 hr. polysaccharide (26·0 g.), and crude mixed metasaccharins (12·3 g.; 10·9 g. after recovery from their filtered acetone solution). From the calcium salts (11·2 g.), prepared and fractionated as described above, were separated, *inter alia*, the β-metasaccharinate (2·4 g.), $[\alpha]_D^{24}$ −23·2° (*c*, 1·17 in H_2O), and the α-salt (4·6 g.), $[\alpha]_D^{24}$ −6·8 (*c*, 1·18 in H_2O). The brucine salt, m. p. 145—148° (Found: N, 5·1. Calc. for $C_{29}H_{38}O_{10}N_2$: N, 4·9%), from the latter showed $[\alpha]_D^{22}$ −24·8° (*c*, 1·13 in H_2O); Nef (*loc. cit.*) gave m. p. 145—150°, $[\alpha]_D^{20}$ −23·1°. Recovered polysaccharide (20 g.), treated as was that from " insoluble " laminarin, yielded polysaccharide (4·8 g.), impure calcium β-metasaccharinate (2·9 g.), $[\alpha]_D^{24}$ −15·6° (*c*, 5·1 in H_2O), and crude calcium α-metasaccharinate (4·2 g.), $[\alpha]_D^{22}$ −6·2 (*c*, 2·1 in H_2O).

No substantial change in the above results ensued on preliminary dialysis of the laminarin against distilled water, followed by treatment with charcoal. Thus after 4 hr. at 100°, in oxygen-free lime-water (0·0415N), the degree of degradation, as measured by acid formation, was constant and amounted respectively for untreated and for treated samples to 39·9 and 33·8% for " insoluble " (I.L.7) and to 19·1 and 19·0% for " soluble " (S.L.5) material.

Hypoiodite chain-length determinations on the samples of laminarin employed above gave values of 42 (I.L.4), 38 (I.L.7), and 72 (S.L.5) respectively, whilst those of the corresponding unreactive materials derived from them were 166, 194, and 114 respectively.

This work forms part of the programme of fundamental research undertaken by the Council of the British Rayon Research Association.

THE BRITISH RAYON RESEARCH ASSOCIATION,
BARTON DOCK ROAD, URMSTON, NR. MANCHESTER. [*Received, November 16th*, 1954.]

Methyl Affinities of Aromatic Compounds.

By C. A. COULSON.

[Reprint Order No. 5963.]

The methyl affinity, recently introduced by Levy and Szwarc to describe reactions of the form Me + A ⟶ MeA, where A is an aromatic molecule, is shown to be closely related to both the atom-localisation energy and the appropriate free valence of A. The analysis predicts the position of addition of the methyl group, and could be used to estimate values of the methyl affinity which have not yet been measured experimentally.

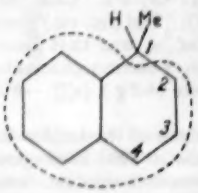
IN a preliminary note, Levy and Szwarc (*J. Chem. Phys.*, 1954, **22**, 1621) have introduced the term " methyl affinity " to describe the ease of addition of a methyl group to aromatic compounds. A typical example would be the reaction:

$$Me + C_6H_6 \longrightarrow Me{\cdot}C_6H_6$$

By comparison of the rates of reaction for different molecules, these authors were able to assign a relative methyl affinity to each member of a series of aromatic compounds, most, but not all, of which were pure hydrocarbons. Numerical values for these affinities were given. It is the purpose of the present paper to show that there is a close relation between Levy and Szwarc's methyl affinity values and certain theoretical magnitudes which have already been found useful in discussions of substitution and addition reactions (see, *e.g.*, Coulson, *Research*, 1951, **4**, 307; R. D. Brown, *Quart. Rev.*, 1952, **6**, 63). The relationships are so close that it would seem to be possible to predict the appropriate affinity values for other aromatic hydrocarbons for which experimental results are not yet

available. At the same time the success of the theory leads to predictions concerning the positions in the aromatic molecules at which the methyl radical attaches itself. In view of the fact that no experimental indications of these positions are reported by Levy and Szwarc, these theoretical considerations may be of some value.

Let us consider the addition of a methyl group to naphthalene. A plausible assumption is that the radical attaches itself to one or other of the carbon atoms. Suppose first that this is position 1 [see (I)]. Then, following the model developed by Wheland (*J. Amer. Chem. Soc.*, 1942, **64**, 900) for substitution reactions, we may suppose that in the final product the bonds around carbon atom $C_{(1)}$ are tetrahedral so that the resonating part of the molecule is now reduced to the region within the dotted lines. The formation of the new bond $C_{(1)}$–Me requires that one π-electron be removed from the conjugating system. It is a reasonable supposition that the only variable part of the energy of formation of (I) as compared with attack at other possible positions such as $C_{(2)}$ or with attack on other hydrocarbon molecules, lies in the loss of resonance energy due to this localisation process. We may therefore expect a correlation between the ease of reaction and the localisation energy just described. It is true that this simple picture ignores both the possibility of an activation energy additional to that involved in breaking the resonance system, and also any entropy effects. It is also probable that hyperconjugation from the attached methyl group, acting as an electron donor, will tend to feed electrons into the residual resonating system and so help to stabilise this " odd-alternant " by partly completing its top half-occupied molecular orbital. But none of these complications would be expected to influence the correlation with localisation energy to any great extent.



(I)

The Figure, curve *a*, which is constructed from the data in the Table shows how closely the relative methyl affinity of an aromatic hydrocarbon is connected with the localisation energy. In this table we have chosen that particular carbon atom in each of the molecules for which the localisation energy is lowest. And we have first divided Levy and Szwarc's index by the number of equivalent positions of attack, so that the figures in the fifth column of the Table show the affinities per effective atom, scaled in such a way that benzene is unity. Curve *a* in the figure shows that there is an almost linear relation between the localisation energy (calculated in terms of the conventional resonance integral β) and the logarithm of the relative affinity per atom. A logarithmic relation of this kind is just what we should have hoped to find if our interpretation of the reaction were correct.

The second column in the Table shows which are the reactive atoms in each molecule. These are very much what we should have expected. But the agreement leaves little doubt about our conclusions. For example, in naphthalene there are three conceivable positions of attack—atoms 1, 2, and 9. The deviations of the localisation energies appropriate to these three positions from the value to be expected from the curve in the Figure are $-0{\cdot}01\beta$, $+0{\cdot}17\beta$, and $+0{\cdot}75\beta$, respectively. If we had chosen any but the first of these three, the theoretical point would be very far off from the line which is drawn in the Figure.

There is a further numerical magnitude with which a correlation might be sought. This is the free valence of the carbon atom under attack. The relative interpretation of free valence and localisation energies has been discussed by Burkitt, Coulson, and Longuet-Higgins (*Trans. Faraday Soc.*, 1951, **47**, 553) and so need not be discussed here. The figures given in that paper being used, the values in the seventh column of the Table are obtained. Again, as curve *b* of the Figure shows, the correlation is excellent. In neither the free valence nor the localisation description is there any inversion in the sequence of values for the molecules listed.

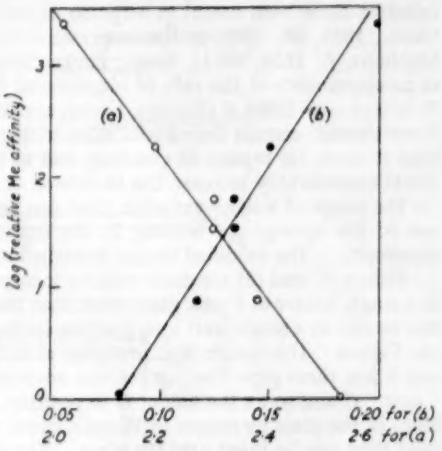
The excellent fit in curves *a* and *b* suggests that calculated localisation energies or free valences could be used to predict methyl affinities for other molecules for which experimental values are not yet available. The equations of the best straight lines in the Figure are :

$$\text{curve } a: \ \log_{10} r = 16{\cdot}66 - 6{\cdot}57\, E_a \text{ and curve } b: \ \log_{10} r = 29{\cdot}44\, F - 2{\cdot}40$$

where r = relative methyl affinity per effective atom, E_a = localisation energy in units of

β, and F = free valence at the point of addition. It is a simple matter to use these equations to predict methyl affinities, though since the calculation of localisation energies for large molecules soon becomes exceedingly tedious, it might be necessary to resort to the simplified calculations of Dewar (*J. Amer. Chem. Soc.*, 1952, **74**, 3357) and Gore (*J.*, 1954, 3166).

In the above discussion no reference has been made to molecules other than hydrocarbons, but there is no reason in principle why the method should not be extended to cover such heterocyclic molecules as pyridine and quinoline, studied by Levy and Szwarc. The best approach would be along the lines laid down in a similar type of discussion by Longuet-Higgins (*J. Chem. Phys.*, 1950, **18**, 283). We have not reported any such calculations here because they require a knowledge of the correct Coulomb terms for the heteroatom and its neighbours, such as we do not yet possess. The free valence correlation, if



(*a*) *Relation between* $\log_{10}$ (*methyl affinity*) *and localisation energy (in units of* β).
(*b*) *Relation between* $\log_{10}$ (*methyl affinity*) *and free valence.*

still applicable, would, however, lead us to expect a small, but definite, increase in methyl affinity on passing from a hydrocarbon (*e.g.*, naphthalene) to a related heterocyclic molecule (*e.g.*, quinolone). This is precisely what Levy and Szwarc have found; and a comparison of the localisation energies for benzene and pyridine (Wheland, *loc. cit.*) suggests a similar conclusion. On this basis we should not expect a great difference between the heterocyclic molecule and its related hydrocarbon.

Molecule	Position of attack	No. of equiv. positions	Observed methyl affinity	Relative methyl affinity per atom	Localisation energy (units of β)	Free valence
Benzene	1—6	6	1	1·0	2·54	0·081
Diphenyl	2	4	5	7·5	2·38	0·118
Naphthalene ...	1	4	22	33	2·30	0·134
Phenanthrene ...	1, 9	4	42	63	2·30	0·134 (9, 10) 0·133 (1, 8)
Pyrene	1, 3	4	125	187	2·19	0·151
Anthracene	9	2	820	2460	2·01	0·202

Observed methyl affinities are due to Levy and Szwarc (*J. Chem. Phys.*, 1954, **22**, 1621). Localisation energies and free valences are taken from the list in Burkitt, Coulson, and Longuet-Higgins (*Trans. Faraday Soc.*, 1951, **47**, 553), except for pyrene, the free valence of which is given by Berthier, Coulson, Greenwood, and Pullman (*Compt. rend.*, 1948, **226**, 1906) and the localisation energy is newly calculated, by the method recently proposed (Coulson, *J.*, 1954, 3111). The author is indebted to Mr. V. W. Maslen for making these calculations.

MATHEMATICAL INSTITUTE, OXFORD [*Received, December 14th*, 1954.]

An Electromagnetic Sorption Balance.

By S. J. Gregg.

[Reprint Order No. 6010.]

An electromagnetic sorption balance is described which permits one to follow the change in weight of a solid either *in vacuo* or when exposed to a gas at a temperature between −200° and 1200° c. A change in weight of up to 4 g. (±0·1 mg.) on 25 g. may be measured.

Earlier (*J.*, 1946, 561), an electrical sorption balance was described, which has proved useful for following the change in weight of a solid, in a vacuum or a gas, maintained at a fixed temperature or subject to a rising temperature, between −200° and 1200°. Such balances have been useful in sorption experiments (*e.g.*, Gregg and Sing, *J. Phys. Colloid Chem.*, 1951, **55**, 597), in thermogravimetric analysis in air or in a vacuum (Gregg and Stephens, *J.*, 1953, 3951; Gregg, Parker, and Stephens, *J. Appl. Chem.*, 1954, **4**, 666), and in measurements of the rate of reactions of the type Solid $A \longrightarrow$ Solid B + Gas, or Solid B + Gas $\longrightarrow$ Solid A (Britton, Gregg, and Winsor, *Trans. Faraday Soc.*, 1952, **48**, 63, 70). Nevertheless, certain drawbacks were encountered; in particular, (1) it is troublesome to take it down for repairs or cleaning, and to reassemble it; (2) the numerous ground-glass joints considerably increase the likelihood of leakage in vacuum or sorption experiments; (3) the range of weight variation that can be studied is rather limited (*ca.* 0·5 g.); (4) the use of the springs for leading in the current to the inner solenoid results in reduced sensitivity. The modified design described now reduces or overcomes these disadvantages.

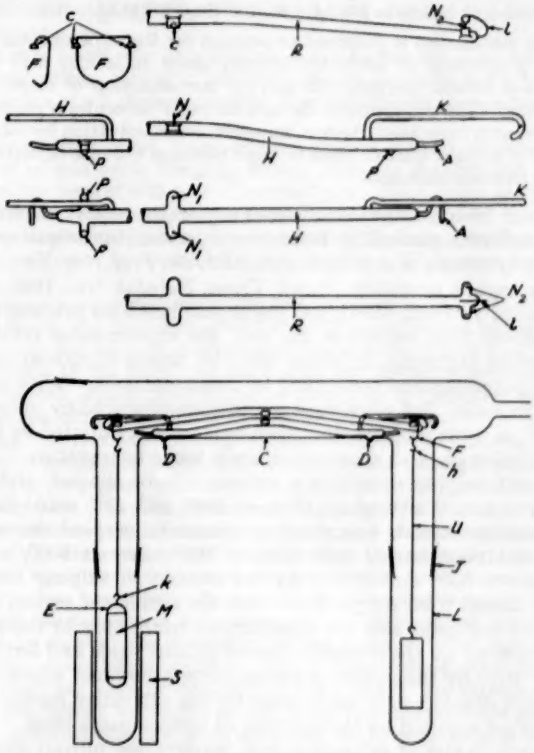
Points (1) and (2) are dealt with by incorporating the main bearing and the arrestments in a single holder of Pyrex glass, such that the balance arm, already mounted on its holder, can be slid as a single unit into position in the balance case. Details will be gathered from the Figure. The holder H is provided at each end with the hooks K for ease of handling, and it has three pips P which register with the corresponding depressions D in the balance "case" C and so fix the holder H in position. The needles N_1 are held in small cylindrical holes in the glass by means of Wood's metal or wax; alternatively, if sapphire needles are used they can be fused into the glass. The arrestments A are formed by drawing out the end of H and bending it so that the movement of the ends of the balance arm R is restricted to 0·8 to 1·2 mm. The balance arm (*ca.* 25 cm. long) is of Pyrex glass and has cups c at the centre and needles N_2 at the two ends, each carrying a stirrup (F) from which hang the leads. The stirrups are made as small as possible, and are prevented from falling off the arm by the loops l of platinum wire, which still permit free movement of the stirrups when the balance is in use. The small platinum hooks h facilitate the otherwise rather delicate operation of hanging the suspension rods U on to the stirrups when the arm is in position.

The inner solenoid of the earlier model is replaced by a cylindrical magnet M (5 cm. × 1 cm.), magnetised along its length and made of Alcomax III, an alloy chosen because its magnetic characteristics are such as to give no appreciable hysteresis effects at the field strengths employed; it is contained in a glass envelope E provided with a hook k. By use of the magnet it is possible to dispense with the lead-in springs of the earlier model, and also to increase the range to several grams with a current through the solenoid S of a few ma at the most. A suitable specification of the solenoid is as follows: a cylindrical former of Paxoline, 80 mm. long by 31 mm. diameter, is wound to a depth of 8 layers with 35 S.W.G. copper wire, double silk covered or enamelled, producing a total resistance of about 100 ohms; with two 2-volt accumulators this coil gives a total range of 4 g. or so. The current should be measured potentiometrically to give a sufficient degree of precision; an ammeter is useful for purposes of indication.

For determination of the null position of the arm an optical projection system has been found more convenient than an optical lever. An enlarged image of some suitable moving part, *e.g.*, the hook k of the glass magnet case, is formed on a ground glass screen carrying a small graduated scale; the null position is then chosen at a fixed distance from one or

other of the two readings obtained when the arm is touching the arrestments. In this way errors due to slight shifts in the optical system or in the position of the balance case are eliminated. Suitable arrangements are : projection lamp 40 w, with a lens of 20 cm. focal length (f) placed approximately 20 cm. in front of it and distant 25 cm. from the hook k; after passing k the light beam passes through a lens ($f = 10$ cm.) placed 6 cm. in front of k, and is brought to a focus on a screen 60 cm. from k; a plane mirror is placed immediately behind k—outside the case—so as to turn the beam into a convenient direction.

The precision of the balance is *ca.* 10^{-4} g., and the zero is reproducible after several days; the calibration, in milliamp. per gram (of the order of 1 mA per g. for the above specification),



in general varies by only one per cent. or so over a period of months, but should be checked at frequent intervals. The total load on each side of the balance can be 50 g. or more, so that the weight of the working substance may be as high as 25 g. or so if necessary.

The now disused lead-in connections on the " bucket " side of the balance may be used for a resistance thermometer or a thermocouple to measure the temperature of the sample. Up to about 450° limb L may be of Pyrex glass, but between 450° and 1000° fused silica or mullite should be used. From 1000° to 1350° mullite is satisfactory, and for making connection with the rest of the balance case may be fused on to a standard joint of Pyrex. At high temperatures it is necessary to protect the joint J by a water-cooled aluminium baffle.

The author thanks Mr. B. Sutton for his patient experimentation on the holder and stirrups, and Messrs. R. C. Asher, R. Stock, J. F. Goodman, and K. H. Hill for testing various features of the balance and the optical system.

UNIVERSITY COLLEGE, EXETER. [*Received, January 4th*, 1955.]

The Kinetics of the Oxidation of Sulphur Dioxide by Nitrous Oxide.

By T. N. Bell, P. L. Robinson, and A. B. Trenwith.

[Reprint Order No. 5984.]

Kinetic studies of oxidation by nitrous oxide are now extended to sulphur dioxide at temperatures between 650° and 736° and pressures of about half an atmosphere. Measurements of the initial rate at various concentrations of the reactants indicate an empirical rate equation of the form:

$$\text{Rate} = k'[N_2O]^{1\cdot45} + k''[N_2O]^{0\cdot52}[SO_2]$$

A reaction mechanism is proposed to account for the experimental results in terms of a splitting of activated nitrous oxide molecules into molecular nitrogen and atomic oxygen, followed by the oxidation of sulphur dioxide by the latter. The activation of the nitrous oxide molecules is predominantly by collision with their like; there is, however, some activation by collision with molecules of sulphur dioxide since in their presence the rate of decomposition of nitrous oxide is increased.

This communication describes the behaviour of nitrous oxide with sulphur dioxide which it oxidises smoothly and homogeneously. Reference to previous investigations which have dealt with the oxidation by nitrous acid of hydrogen (Melville, *Proc. Roy. Soc.*, **1933**, *A*, **142**, 524; 1934, *A*, **146**, 737), carbon monoxide (Bawn, *Trans. Faraday Soc.*, **1935**, **31**, **461**), methane (Robinson and Smith, *J.*, **1952**, 8395), and the *n*-paraffins from propane to nonane (Smith, *J.*, 1953, 1271), shows that, except in the last, the experimental results can be readily ascribed to a reaction beginning, at about 600°, by fission of nitrous oxide into nitrogen molecules and oxygen atoms and continuing by chain reactions. With methane the chains include free alkyl radicals; but when such radicals are produced by pyrolysis of the hydrocarbon below 600°, as with propane, etc., then oxidation is initiated by their attack on the nitrous oxide, and takes place at a correspondingly lower temperature.

The reaction with sulphur dioxide was expected to be simpler, and, as no chains are involved, has proved so. Whittingham (*Nature*, **1947**, **159**, 232) noted that, in the presence of nitrous oxide, sulphur dioxide is oxidised at a measurable speed above 550°; this agrees with our finding oxidation barely detectable at 500°, slow at 600°, and convenient for measurement between 650° and 750°. As the amount of sulphur trioxide formed was small and oxygen absent from the products over the significant region, dissociation of the trioxide was clearly negligible and the observations relate only to the oxidation reaction. The rate depends mainly on the concentration of nitrous oxide and but slightly on that of sulphur dioxide. Broadly the picture is one of decomposition of nitrous oxide followed by oxidation of sulphur dioxide, as is made clear by the activation energy of the initial step approximating to that required for the splitting of nitrous oxide itself. But other factors, such as the different modes of activating and deactivating nitrous oxide molecules, and the reactions between oxygen atoms and nitrous oxide molecules, and between oxygen atoms themselves at a surface, must detract somewhat from the essential simplicity. Of these factors, the only one effective enough to demonstrate its presence in our rate measurements is the activation of nitrous oxide molecules by collision with sulphur dioxide molecules. The initial rates of reaction in mixtures of sulphur dioxide and nitrous oxide are appreciably greater than the rate of decomposition of nitrous oxide alone. Sulphur dioxide is of course by no means the only gas bringing about this activation (Volmer and Bogden, *Z. phys. Chem.*, **1933**, *B*, **21**, 257; Lewis and Hinshelwood, *Proc. Roy. Soc.*, **1938**, *A*, **168**, 441).

Experimental

Materials.—(i) Sulphur dioxide, the middle portion from a siphon of liquid, was dried (P_2O_5) and collected in a trap cooled in liquid nitrogen. After any non-condensable gas had been removed by pumping, the sample was fractionated between traps maintained at −72° and −196°, head and tail fractions being discarded.

(ii) Nitrous oxide, from a cylinder of anæsthesia-grade gas, was washed with concentrated pyrogallol solution, dried (P_2O_5), and frozen in a trap cooled in liquid nitrogen. Non-condensable gases were removed by pumping, and the material was further purified by fractionation between traps kept at $-130°$ and $-196°$, the first and last portions being rejected.

The nitrous oxide and sulphur dioxide were separately stored in three-litre glass containers each of which was connected to its own one-litre sampling bulb.

Apparatus.—Two cylindrical, silica reaction vessels were used; an unpacked one, 19 cm. × 4·5 cm., with a surface : volume ratio of 1·81 : 1, and another, 4 cm. × 11 cm., packed with silica tubing, with a surface : volume ratio of 9·5 : 1. Each vessel had a thermocouple well and a capillary inlet which was fitted with a ground socket to connect it to the rest of the system. This was constructed of "Pyrex" glass, and was attached to a mercury-vapour pump backed by a rotary oil-pump.

In use, the reaction vessel was embedded in a well-lagged, tubular, electric furnace. The temperature was kept within $\pm 1°$ by a "Sunvic" energy regulator and a hot-wire switch, and was measured by means of a "chromel-alumel" thermocouple in conjunction with a "Doran" potentiometer.

For charging the reaction vessel, a two-way tap enabled it to be connected in turn with the sulphur dioxide and nitrous oxide sampling bulbs. Between this tap and the reaction vessel was a manometer in the form of a U-tube of narrow bore. Dead space was kept to a minimum and maintained at 100° to prevent the condensation of sulphur trioxide.

The more readily condensable products were removed through a capillary tap to a series of traps where they were frozen by means of liquid nitrogen. What remained was absorbed on activated charcoal.

The analysis apparatus consisted essentially of a gas burette, capable of measuring volumes of from 0·01 ml. to 30 ml. with an accuracy of 0·1%. It could be used either as a Töepler pump or a McLeod gauge, and was connected to two adsorption bulbs in such a way that gas could be passed from the burette to the bulbs and back again for further measurement. Oxygen was removed by finely divided copper, precipitated on kieselguhr as described by Meyer and Ronge (*Angew. Chem.*, **1939**, **52**, 637), and sulphur dioxide by "Carbasorb."

Operation.—Since the reaction between sulphur dioxide and nitrous oxide involves no pressure change, its progress was followed by analysing the mixtures obtained after various times of heating. The two gases were introduced into the reaction vessel in turn from the appropriate sampling bulb, the interval between the successive additions being within 5 sec. After a heating-time measured to ± 5 sec., the products were respectively frozen out or absorbed in the collecting traps. The condensable materials were first partially separated by fractionation between traps, the nitrous oxide and sulphur dioxide being taken off at $-72°$. The volume of this mixture was measured in the gas burette; the sulphur dioxide was then absorbed on "Carbasorb" and the decrease in volume measured. Oxygen was removed from the non-condensable portion by copper; the remaining gas was assumed to be nitrogen.

Analytical Results.—Complete analyses of the products formed after heating mixtures of nitrous oxide (100 mm.) and sulphur dioxide (100 mm.) at 697° for various times showed that the volume of nitrogen formed was equal to the volume of nitrous oxide and sulphur dioxide which had reacted, provided that not more than half the sulphur dioxide had been oxidised; within this limit no oxygen was found in the non-condensable products. A trace of oxygen was, however, detected when the reaction had proceeded beyond the half-way point. These results showed that the amount of nitrogen formed was an accurate measure of the extent of the reaction. Once this was established only nitrogen was determined. Composition–time curves, comprising all the components except sulphur trioxide, are given in Fig. 1.

Order of Reaction.—A series of experiments, in which the initial pressure of one reactant was fixed and that of the other varied, was made at four different temperatures. The amounts of nitrogen formed in the individual mixtures after various times of heating were measured and plotted against time. The graphs were smooth curves from which the initial rates of reaction were estimated. The effects on these rates of varying the concentrations of nitrous oxide and sulphur dioxide are shown in Figs. 2 and 3, respectively. From the graphs, it is seen that the order of reaction with respect to nitrous oxide is greater than unity, and that it is dependent on the first power of the concentration of sulphur dioxide. The curves are similar in form to those obtained by Robinson and Smith (*loc. cit.*) for the reaction between nitrous oxide and methane, and yield the following empirical equation for the rate of reaction :

$$\text{Rate} = k'[N_2O]^x + k''[N_2O]^y[SO_2]$$

Changes in the concentration of sulphur dioxide have markedly less effect on the initial rates of reaction than corresponding changes in the concentration of nitrous oxide; hence the contribution of the second term in the above equation to the overall rate of reaction must be small. When the contribution of the second term is neglected, logarithmic plots of initial rates against

FIG. 1. *Composition–time curve at* 697° C.

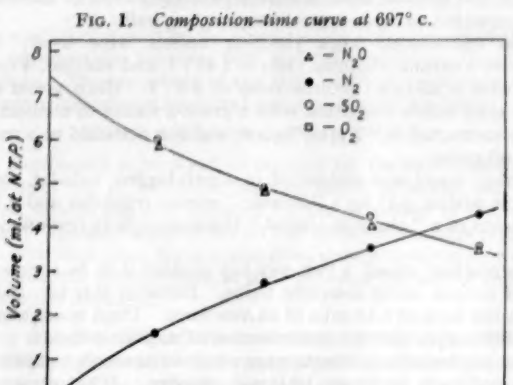


FIG. 2. *Influence of pressure of nitrous oxide on initial rate (sulphur dioxide pressure = 100 mm).*

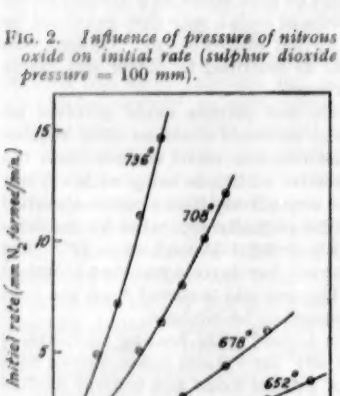
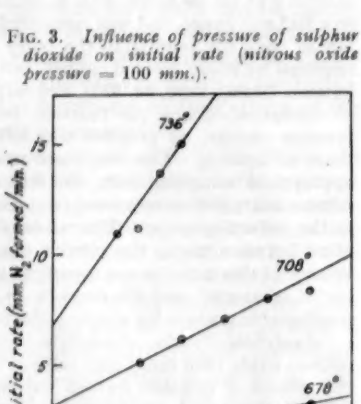


FIG. 3. *Influence of pressure of sulphur dioxide on initial rate (nitrous oxide pressure = 100 mm.).*



nitrous oxide concentrations give the following values for x at the temperatures specified: 1·47 (652°); 1·43 (678°); 1·46 (708°); 1·43 (736°); mean 1·45. To obtain y, plots were made of the initial rate against sulphur dioxide concentration for two different, fixed concentrations of nitrous oxide at 678°. The ratio of the slopes of these lines corresponds to $[N_2O']^y/[N_2O'']^y$, $[N_2O']$ and $[N_2O'']$ being the two nitrous oxide concentrations. From these data y proved to be 0·58, making the empirical rate equation:

$$\text{Rate} = k'[N_2O]^{1\cdot45} + k''[N_2O]^{0\cdot58}[SO_2]$$

Activation Energy.—The intercepts in Fig. 3 correspond to $k'[N_2O]^{1\cdot45}$. Plotting the log of the intercept against $1/T$, and taking into account the variation of pressure with temperature gave the activation energy E' a value of 56 kcal.

The slopes of the lines in Fig. 3 correspond to $k''[N_2O]^{0.58}$. From a plot of log of the slope (corrected for the variation of pressure with temperature) against $1/T$, the activation energy E'', correspodning to k'', was found to be 70 kcal.

Effect of Surface Area.—In a number of runs, a packed reaction vessel with a surface : volume ratio approximately five times that of the unpacked vessel was used. This change had no measurable effect on the rates of reaction.

Discussion

The reaction between sulphur dioxide and nitrous oxide is similar to that between methane and nitrous oxide, and the empirical rate equations bear a close resemblance to one another. In each, the first term is almost identical with the empirical expression for the decomposition of nitrous oxide. At our experimental pressures and 652°, the rate of decomposition of nitrous oxide alone is proportional to $[N_2O]^{1.55}$ (Lewis and Hinshelwood, *Proc. Roy. Soc.*, 1938, *A*, **168**, 441), an order with respect to nitrous oxide slightly greater than that given by our experiments. The difference probably arises from the approximation made in calculating the value for x, namely the neglect of the contribution of the second term to the overall rate. Incidentally, the activation energy, E', associated with the first term is significantly close to that for the thermal decomposition of nitrous oxide alone (for which Lewis and Hinshelwood obtained values of 55·3 and 57·1 kcal., from the decomposition at 100 mm. pressure). Thus there is good evidence that the first term concerns the decomposition of nitrous oxide itself.

The initial rate of the reaction, as Fig. 3 shows, increases linearly with the concentration of sulphur dioxide. The reasonable assumption being made that the oxidation, $O + SO_2 \longrightarrow SO_3$, is fast, and independent of the concentration of sulphur dioxide (provided that there is an excess), it follows that the rate of formation of sulphur trioxide must depend solely upon the availability of oxygen atoms. These atoms are derived from the decomposition of active nitrous oxide molecules and we believe the observed increase in rate, following an increase in sulphur dioxide concentration, is attributable to the latter's participation in the activation of nitrous oxide. Increases in the rate of decomposition of nitrous oxide in the presence of a number of other gases have been ascribed to this cause. We therefore propose the following mechanism for the reaction :

$$N_2O + N_2O = N_2O^* + N_2O \quad \ldots \quad (1)$$
$$N_2O + SO_2 = N_2O^* + SO_2 \quad \ldots \quad (2)$$
$$N_2O^* + N_2O = N_2O + N_2O \quad \ldots \quad (3)$$
$$N_2O^* + SO_2 = N_2O + SO_2 \quad \ldots \quad (4)$$
$$N_2O^* = N_2 + O \quad \ldots \quad (5)$$
$$O + SO_2 = SO_3 \quad \ldots \quad (6)$$
$$O + O + M = O_2 + M \quad \ldots \quad (7)$$
$$O + N_2O = N_2 + O_2 \quad \ldots \quad (8)$$
$$O + N_2O = 2NO \quad \ldots \quad (9)$$

(A rate constant carries the serial number of the equation to which it refers.)

Since the amount of molecular oxygen formed during the reaction is very small, and as no nitric oxide was detected at any time, reactions (7), (8), and (9) must be extremely slow compared with (6), and may safely be neglected. From the usual stationary state conditions we then have

$$\text{Rate} = \left\{k_1[N_2O]^2 \Big/ \left(1 + \frac{k_3}{k_5}[N_2O] + \frac{k_4}{k_5}[SO_2]\right)\right\} + \left\{k_2[N_2O][SO_2] \Big/ \left(1 + \frac{k_3}{k_5}[N_2O] + \frac{k_4}{k_5}[SO_2]\right)\right\}$$

If k_4 were comparable in magnitude with k_3, then the order of reaction with respect to sulphur dioxide would be expected to be less than unity. The straight-line plots in Fig. 3

show that this is not so, and hence k_4 must be appreciably less than k_3. The above expression may therefore be simplified to:

$$\text{Rate} = k_1[N_2O]^2 \Big/ \left\{1 + \frac{k_3}{k_5}[N_2O]\right\} + k_2[N_2O][SO_2]\left\{1 + \frac{k_3}{k_5}[N_2O]\right\}$$

This equation approaches closely the form of the empirical rate equation. The first term is the same as that for the decomposition of nitrous oxide alone and corresponds to $k'[N_2O]^{1\cdot45}$. The second term in the theoretical rate expression can thus be written in the form $k_2k'/k_1\{[N_2O]^{0\cdot45}[SO_2]\}$. This predicts an order with respect to nitrous oxide in the second term near to that found experimentally. It is to be noted that, taking a value of 1·55 for the order with respect to nitrous oxide in the first term, we obtain a much closer agreement between the empirical and theoretical orders for nitrous oxide in the second term. The empirical rate constant k'' is identified with k_2k'/k_1, and hence $E_2—E_1 =$ 14 kcals. Although small, the difference between the activation energies of the two reactions is not readily accounted for. It has been pointed out that the thermal decomposition of nitrous oxide is not a simple process, and that the complexity may be due to the occurrence of more than one quasi-unimolecular reaction, each involving a different mode of activation and a different transformation probability of the activated molecules (Hinshelwood, "Kinetics of Chemical Change," Oxford Univ. Press, 1940, p. 131). It is not unlikely that the two activation energies may owe their difference to the two types of molecular collision involved and the modes of activation resulting from them.

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Studies in the Chemistry of Quadrivalent Germanium. Part II. The Depolymerisation of the Pentagermanate Ion with Change of* pH, *and Ion-exchange Studies of Germanate Solutions containing Sulphate and Orthophosphate.*

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An extension of the studies previously reported has shown that in solutions of pH less than 9 the pentagermanate ion is replaced by a less complex ion, probably monogermanate. This replacement proceeds to an increasing extent with fall in pH, at least down to pH 4. The less complex ion is not so firmly sorbed by anion-exchange material and is more readily displaced from it by chloride ion added to the solution than is the pentagermanate ion.

For solutions containing germanate and either sulphate or phosphate in the pH range 7—9·5 it has not proved possible to interpret the results of anion-exchange experiments in terms of the sorption of germanate ions and of sulphate or phosphate ions as such. The results are consistent, however, with the sorption of germanate ions (either mono- or penta-germanate) together with either $[GeO_3(SO_4)]^{2-}$ or $[HGeO_3(PO_4)]^{3-}$ ions. Evidence is thus obtained for the formation of two new complex acids of quadrivalent germanium.

THE work reported in Part I * on the sorption of germanate ions by an anion-exchange material from solutions containing chloride has been extended and the results of similar experiments with solutions containing germanates and either sulphates or phosphates are

* Part I, *J.*, 1954, 2438.

also reported. In these last two cases, it has not proved possible to interpret the results in terms of the sorption of sulphate (or phosphate) ions and mono- or penta-germanate ions, and the formation of complex anions is indicated. This complex-formation seems to occur over the same range of pH as the formation of pentagermanic acid, and the two reactions proceed side by side. Both species are sorbed by the exchange material, but the sorption of the pentagermanate ion occurs to a greater extent and so the sorption of germanium at the various pH values follows much the same pattern as in the experiments with chloride.

Experimental

The ion-exchange resins, the method of preparing the solutions, and the experimental procedure were all as in Part I (*loc. cit.*). It was observed, however, in one series of experiments that equilibrium was reached after the solutions and resin had been shaken mechanically for 8 hr. daily for 3 days.

Analytical Methods.—Sulphate was determined gravimetrically as barium sulphate after elution from the resin with 500 ml. of 2N-hydrochloric acid; excess of the eluting agent was first removed by evaporation of the solution and care was taken to avoid loss of sulphate. Phosphate was determined gravimetrically as phosphomolybdate; the resin was well washed with water to remove the bulk of the sorbed germanate before the phosphate was eluted with 2N-nitric acid (500 ml.). The amount of germanium present in the solutions used for the phosphate estimation was thus very small and it has already been shown that small quantities of germanium do not interfere in this determination (Everest, *J.*, 1953, 4117). Germanium was determined iodometrically as before (*idem, ibid.*), and chloride gravimetrically as silver chloride. The capacities of the resin samples were determined as before (Part I, *loc. cit.*).

Results.—Equilibrium experiments with solutions containing chloride. The quantities of germanium and chloride sorbed by the resin in experiments with 1·5 mmoles of germanium and 0·7 mmole of chloride present (that present as the chloride form of the resin being included) are shown in Table 1, together with the number of germanium atoms present in 1 equiv. of the germanate ions sorbed (=R). It is apparent from these results that the values found for R lie between those previously found (Part I, *loc. cit.*) for solutions containing no added chloride and those found for solutions containing equimolecular amounts of chloride and germanium (Part I). As in the former case, the values of R fall with decrease in pH, but not to quite the same extent.

From the preceding and the present work it is clear that, at any given pH value, as the chloride concentration in the solution increases, the sorption of chloride by the exchange

Table 1. *Sorption of germanium and chloride from solutions (75 ml.) containing 1·5 mmoles of germanium by* I.R.A.-400-Cl (0·25 *g.*) *with 0·7 mmole of total chloride present.*

Soln. pH	Moles sorbed per equiv. of resin: Ge	Cl	R_{Ge} *	Method	Soln. pH	Moles sorbed per equiv. of resin: Ge	Cl	R_{Ge} *	Method
4·54	0·081	0·858	0·57	*a*	7·64	1·22	0·481	2·35	*a*
6·00	0·416	0·769	1·80	*a*				2·57	*b*
6·64	0·737	0·688	2·36	*a*	8·64	1·63	0·395	2·74	*a*
								2·54	*b*

* R = No. of germanium atoms in 1 equiv. of the germanate ions sorbed; the methods of calculating R are given in Part I.

material goes up whilst that of the germanium goes down. Since exchange proceeds by equivalents, it is evident that each equivalent of chloride sorbed by the resin will displace one equivalent of sorbed germanate. Thus by comparing the changes in the amounts of germanium and chloride sorbed at corresponding pH values in the various series of experiments with differing amounts of chloride present (Fig. 1, Part I, and Table 1, Part II) values of R may be derived (called R' in Table 2 for convenience in discussion). Three sets of values have been obtained (Table 2) from the different series (the curves referred to are those of Fig. 1, Part I): (1) By method (*d*), comparison of the results given in Table 1 with corresponding results obtained by interpolation from curve *a*. (2) By method (*e*), comparison of results plotted in curves *c* and *d* with corresponding results interpolated from curve *a*. (3) By method (*f*), comparison of results from curves *c* and *d* with those in Table 1. To compare the results at corresponding pH values interpolated results have been used.

Column experiments. In addition to the usual batch experiments used in this work, some studies were made of the sorption of germanium from solutions passed through columns of the resin I.R.A.-400-Cl. It was assumed that the chloride liberated, and hence present in the effluent, was equivalent to the germanium sorbed (cf. method *b* for determining *R* in Part I), and mean values of *R* for the germanate ions sorbed were calculated. The results are given in Table 3. In all cases the pH of the effluent was markedly lower than that of the entering liquid.

TABLE 2. *Number of germanium atoms* (R′) *in* 1 *equiv. of the germanate ions displaced from the resin by chloride ions at various* pH *values.**

Method *d*				Method *e*				Method *f*			
pH	*R′*	pH	*R′*	pH	*R′*	pH	*R′*	pH	*R′*	pH	*R′*
4·54	0·43	7·00	1·58	6·92	1·74	9·34	2·52	7·00	2·09	7·64	2·19
6·00	1·41	7·64	1·68	7·54	1·69	9·86	2·22	7·50	2·11	8·00	2·77
6·64	1·46	8·64	2·05	8·38	1·91	10·08	1·92				
				9·00	2·61	10·42	1·58				

* See p. 1445 for methods.

TABLE 3. *Sorption of germanium from germanate solutions* (75 *ml.*) *by columns of* I.R.A.-400-Cl.

Entering liquid: Ge (mmoles)	pH	Ge sorbed (mmoles)	Cl liberated (mmoles)	*R*	Entering liquid: Ge (mmoles)	pH	Ge sorbed (mmoles)	Cl liberated (mmoles)	*R*
2·505	8·52	1·08	0·529	2·04	1·450	9·40	1·32	0·71	1·86
2·505	9·16	2·24	0·97	2·31	1·450	9·68	1·35	0·88	1·54

TABLE 4. *Sorption of germanium and of sulphate from solutions* (75 *ml.*) *by* I.R.A.-400-SO_4 (0·25 *g.*).

pH of solutions	Ge sorbed: moles/equiv. resin	Ge sorbed: $X = Ge/R_{Ge}$ (equivs.)	Ge sorbed: $X' = Ge/2{\cdot}5$ (equivs.)	SO_4 sorbed (moles/equiv. resin)	Total equivs. sorbed in terms of: Simple ions $X + SO_4$	Simple ions $X' + SO_4$	Complex * + sulphate (s) or germanate	Complex * + sulphate (s) or pentagermanate
			(*a*) 1·67 mmoles of Ge, 1·85 mmoles of sulphate present					
7·44	0·280	0·145	0·112	0·502	1·185	1·15	† 1·00 (s)	
7·80	0·503	0·234	0·201	0·428	1·09	1·06	† 1·03	0·89
8·44	1·086	0·462	0·434	0·376	1·13	1·19	1·06	† 1·04
8·94	1·467	0·587	0·587	0·316	1·22	1·22	1·09	† 1·09
9·40	1·24	0·498	0·498	0·326	1·15	1·15	1·06	† 1·06
			(*b*) 1·67 mmoles of Ge, 0·65 mmole of sulphate present					
7·31	0·359	0·179	0·144	0·447	1·07	1·04	0·894 (s)	
8·34	1·289	0·555	0·516	0·364	1·28	1·24	1·17	† 1·10
9·04	1·527	0·611	0·611	0·292	1·195	1·195	1·08	† 1·08
9·70	1·211	0·515	0·496	0·279	1·07	1·05	1·06	0·93
			(*c*) 1·67 mmoles of Ge, 0·45 mmole of sulphate present					
6·91	0·175	0·094	0·071	0·471	1·04	1·01	0·94 (s)	
7·00	0·297	0·160	0·119	0·464	1·09	1·05	0·93 (s)	
7·46	0·657	0·324	0·263	0·402	1·13	1·06	1·12	0·91
7·90	1·202	0·546	0·481	0·312	1·17	1·105	1·09	† 0·98
8·62	1·402	0·572	0·561	0·300	1·17	1·16	1·06	† 1·04
9·20	1·604	0·642	0·642	0·272	1·19	1·19	1·08	† 1·08
9·64	1·399	0·595	0·560	0·266	1·13	1·09	1·07	† 0·985
10·00	1·114	0·534	0·446	0·316	1·12	1·05	1·10	0·96
10·40	0·707	0·399	0·283	0·350	1·10	0·98	1·20	0·84
			(*d*) 1·66 mmoles of Ge, 0·35 mmole of sulphate present					
6·14	0·358	0·199	0·143	0·478	1·16	1·10	† 0·96 (s)	
7·10	0·778	0·421	0·311	0·412	1·245	1·135	1·28	† 0·95
8·18	1·134	0·558	0·526	0·295	1·16	1·12	1·11	† 1·00
8·64	1·543	0·629	0·617	0·261	1·15	1·14	1·06	† 1·04
9·10	1·642	0·657	0·657	0·259	1·175	1·175	1·07	† 1·07
9·58	1·545	0·672	0·618	0·257	1·19	1·13	1·095	† 1·03
10·26	1·084	0·536	0·434	0·259	1·15	0·95	1·06	0·85
10·58	0·790	0·494	0·316	0·312	1·12	0·94	1·17	0·82
10·86	0·380	0·316	0·152	0·347	1·01	0·85	1·47	0·71

* Complex ion postulated = $[GeO_3(SO_4)]^{3-}$.
† Here there is better agreement with the ideal capacity if sorption of the complex is postulated.

Experiments with added sulphate. The quantities of germanium and sulphate sorbed from solutions (75 ml.) of varying pH, containing 1·5 mmoles of germanium and with 0·35, 0·45, 0·65, and 1·85 mmoles of sulphate present (as sulphate form of the resin and as sodium sulphate) are given in Table 4. In all cases the sorption of germanium reached a maximum, and that of the sulphate a minimum, at pH 9. Below *ca.* pH 6, depending on the sulphate concentration, the sorption of germanium fell to zero. At any given pH the amount of germanium sorbed decreased with increasing concentration of sulphate in the solution. It was found as before (Part I, *loc. cit.*) that the sorbed germanium could be eluted from the resin with distilled water.

Experiments with added orthophosphate. The quantities of germanium and phosphate sorbed by the resin from solutions (75 ml.), of varying pH, containing 1·6—1·8 mmoles of germanium and with 0·40, 1·90, and 4·15 mmoles of phosphate present (as the phosphate form of the resin and as sodium phosphate) are shown in Table 5. The sorption of germanium was again

TABLE 5. *Sorption of germanium and of phosphate from solutions (75 ml.) by* I.R.A.-400-PO_4 (0·25 *g.*).

	Ge sorbed			PO_4 sorbed			Total equivs. sorbed in terms of: Simple Ions		Complex ‡ + phosphate (p) or penta-germanate	
pH of solutions	moles/equiv. resin	X = Ge/R_{Ge} (equivs.)	X' = Ge/2·5 (equivs.)	PO_4 (moles/equiv. resin)	R_{PO_4}* (moles/equiv. resin)	Y = PO_4/R_{PO_4} (equivs.)	$X + Y$	$X' + Y$	germ-anate	
				(*a*) 1·5—1·8 mmoles of Ge, 4·15 mmoles of phosphate present						
5·22	0	—	—	0·853	0·85	1·00	1·00	1·00	1·00 (p)	
6·24	0	—	—	0·709	0·72	0·98	0·98	0·98	0·98 (p)	
6·66	0·043	0·025	0·017	0·665	0·67	0·99	1·02	1·01	1·01 (p)	
6·96	0·139	0·075	0·056	0·626	0·63	0·99	1·07	1·05	1·05 (p)	
7·26	0·308	0·157	0·123	0·523	0·595	0·88	1·04	1·00	0·98 (p)	
7·80	0·728	0·339	0·291	0·426	0·53	0·80	1·14	1·09	0·99 †	0·97
8·84	1·472	0·591	0·589	0·241	0·495	0·49	1·08	1·08	0·98 †	0·97
9·12	1·544	0·605	0·618	0·243	0·485	0·50	1·11	1·12	1·00 †	1·01
9·49	1·450	0·580	0·580	0·232	0·48	0·48	1·06	1·06	0·95 †	0·95
10·10	0·790	0·395	0·316	0·323	0·47	0·69	1·08	1·00	0·88	0·84
10·58	0·192	0·128	0·077	0·428	0·45	0·95	1·08	1·03	0·91 (p)	
11·24	0·023	0·029	0·009	0·403	0·39	1·03	1·06	1·04	1·02 (p)	
				(*b*) 1·68 mmoles of Ge, 1·90 mmoles of phosphate present						
6·55	0·098	0·057	0·039	0·599	0·685	0·87	0·93	0·91	0·93 (p)	
6·98	0·351	0·189	0·140	0·508	0·625	0·81	1·00	0·95	0·95 (p)	
7·36	0·640	0·320	0·256	0·441	0·58	0·76	1·08	1·02	0·98	0·96
7·78	1·038	0·483	0·415	0·343	0·53	0·65	1·13	1·06	† 1·01	0·96
8·24	1·398	0·608	0·559	0·287	0·50	0·57	1·18	1·13	1·06 †	1·02
9·46	1·550	0·620	0·620	0·221	0·48	0·46	1·08	1·08	0·97 †	0·97
9·96	1·011	0·481	0·404	0·269	0·475	0·57	1·05	0·97	0·89	0·84
				(*c*) 1·68 mmoles of Ge, 0·40 mmole of phosphate present						
7·09	1·128	0·594	0·451	0·406	0·615	0·66	1·25	1·11	1·19 †	1·10
8·04	1·469	0·659	0·588	0·259	0·51	0·51	1·17	1·10	1·06 †	1·00
8·99	1·833	0·727	0·733	0·160	0·49	0·33	1·05	1·06	0·98 †	0·99

* R_{PO_4} = moles of PO_4 sorbed per equiv. of resin under the same conditions, but in the absence of germanium. When pH of solutions was less than 7 some phosphate was eluted from resin on washing; this was determined in both cases (*i.e.*, Ge present and Ge absent) and the appropriate corrections made.

† Here there is better agreement with the ideal capacity if sorption of the complex ion is postulated.

‡ Complex ion postulated = $[HGeO_3(PO_4)]^{2-}$.

greatest at pH 9·0—9·2, but, whilst that of phosphate passed through a minimum at this point, there was an overall trend towards a lower degree of sorption with rise of pH. That this last was due to progressive sorption of HPO_4^{--} and PO_4^{3-} ions in place of $H_2PO_4^-$, is apparent from the blank experiments carried out with phosphate alone (see footnote to Table 5). As before, the germanium sorbed by the resin could be eluted with distilled water.

DISCUSSION

Experiments with Added Chloride.—The values of R given in Table 1, taken in conjunction with those previously reported (Part I) for solutions with no added chloride, indicate the sorption below pH 9 by the exchange material of a lower polymer or of the

monomer of the germanate ion together with the pentagermanate ion. It is evident that the less complex acid is sorbed to an increasing extent as the pH is lowered, and this behaviour is consistent with a progressive depolymerisation of the pentagermanate ion. Further evidence is provided by the values of R' quoted in Table 2. As pointed out in Part I, no evidence has yet been forthcoming to show that intermediate polymeric ions such as $Ge_4O_9^{--}$ or $Ge_2O_5^{--}$ exist in solutions in this range of pH, and it is concluded that the less complex ion formed is in fact the monogermanate ion—a conclusion in agreement with the views of Souchay (*Bull. Soc. chim.*, 1953, 395) and of Schwarz and Huf (*Z. anorg. Chem.*, 1931, **203**, 395).

Some further support for such a change in the extent of polymerisation of the germanate ion with pH is provided by the recent observation by Tchakarian and Wallace (*Bull. Soc. chim.*, 1954, 1067) that a precipiate of thallous pentagermanate could be obtained on mixing a thallous nitrate solution (1%) with a germanium dioxide solution (0·04M) only if the pH of the solution was raised by addition of ammonia.

Although they were based on experiments in which equilibrium conditions were not reached—and hence are not so readily interpreted—the results quoted for the column experiments in Table 3 provide, albeit qualitatively, still further evidence for the sorption of a less complex germanate ion than the pentagermanate.

It is apparent from the results given in Part I and in Tables 1 and 2 that the values found for R (and R') at a given pH (in the range 4—9) increase with the concentration of chloride in the solutions—thus the values of R' determined by the method *f* are significantly higher than those determined by methods *d* or *e* (Table 2). Hence, it may be concluded that the monogermanate ions are more readily displaced from the resin by chloride ions than are the pentagermanate ions. This probably arises, at least partly, from the fact that monogermanic acid is the weaker acid, since at pH values above 9, where this acid would be more fully ionised, the effect of the presence of chloride is less marked.

Experiments with Added Sulphate and Orthophosphate.—Attempts have been made to account for the capacity of the resin samples used in terms of the sorption of germanate ions and either sulphate or phosphate ions (Tables 4 and 5). In calculating the equivalents of germanate sorbed, two extreme possibilities have been considered, *viz.*, (1) that the germanium is sorbed as a mixture of mono- and penta-germanate ions in the same ratio as by the hydroxide form of the resin from solutions of the same pH but containing no other anions (as reported in Part I), the equivalents of germanate sorbed then being given by X = (moles of Ge sorbed per equiv.)/R_{Ge}; and (2) that the germanium is sorbed entirely as pentagermanate, the equivalents so sorbed being given by X' = (moles of Ge sorbed per equiv.)/2·5. The results of the experiments in which chloride ion was present have already indicated that the correct value to be employed—which depends on the value of R to be used when a second anion is present—will be between those given by X and by X'.

It has been assumed that the sulphate ion was sorbed as the SO_4^{--} ion over the pH range studied here, but in the case of phosphate it proved necessary to take into account the effect of pH on the species sorbed, and this has been determined in a series of blank experiments over the same ranges of pH and phosphate concentration, but with no germanium present (giving the values of R_{PO_4}; Table 5).

From the results of the calculations, which are given in Tables 4 and 5, it is evident that the capacities calculated in this way [$(X + SO_4)$ or $(X' + SO_4)$ and $(X + Y)$ or $(X' + Y)$] are in good agreement (*i.e.*, within $\pm 5\%$) with the ideal value of 1 equiv. sorbed per equiv. of resin for pH values below 7 and over 9 or 10. Between pH 7 and about pH 9 a significant deviation from the ideal value is found, but in this range the capacities may be accounted for by assuming instead the sorption of the complex ions $[GeO_2(SO_4)]^{--}$ or $[HGeO_2(PO_4)]^{--}$, together with free germanate, sulphate, or phosphate. The method of calculating the capacities in this case follows closely that employed by Jameson and Salmon (*J.*, 1954, 4013).

Of all the possible complexes that can be formed between sulphate and mono- and penta-germanate ions only the $[GeO_2(SO_4)]^{--}$ ion accounts satisfactorily for the resin capacities. The number of complexes which can be formed between the tribasic phosphoric acid and the various germanic acids is high, and products are acids of potentially high

basicity, so the number of possible ions that may be sorbed is great. However, the assumption of the sorption of ions derived from pentagermanic acid {*e.g.*, $[Ge_5O_{10}(PO_4)]^{3-}$ or $[Ge_5O_4(PO_4)_7]^{9-}$} does not lead to satisfactory values for the resin capacity. Thus, a complex derived from monogermanic acid seems to be indicated, and by analogy with the germanate–sulphate system a 1 : 1 complex might be expected. The postulation of the sorption of the $[HGeO_2(PO_4)]^{2-}$ ion does in fact make it possible to account satisfactorily for the resin capacity in the pH range where the sorption of simple ions does not.

The fact that the complex-formation between monogermanic acid and sulphate or phosphate ion occurs over essentially the same pH range as the condensation of monogermanic acid to give pentagermanic acid, suggests that both processes are favoured by the same conditions. In fact, both appear to proceed side by side, for the sorption of both complexes appears to be accompanied by the sorption of free germanate, as pentagermanate (Tables 4 and 5). It thus appears that in this pH range monogermanic acid can condense with other oxy-anions as well as with itself. The extent to which condensation occurs with a second oxy-anion (not germanate) seems to be limited, however, and does not appear to proceed to a stage comparable with the formation of the pentagermanate ion.

Since, in our experiments, a large proportion of the germanium initially present in solution was sorbed by the exchange material—owing to the comparatively low solubility of germanium dioxide and the high sorption of germanium on the resin—and since the resin may show some selectivity towards sorption of the complex ions, it is not possible to assess, even qualitatively, the extent to which the complexes are formed in the solutions. Nevertheless, the fact that the sorption of such complexes occurs at all throws new light on the complex chemistry of quadrivalent germanium.

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The Kinetics and Mechanism of the Reaction of Potassium Ferrocyanide and Nitrosobenzene catalysed by Mercuric and Mercurous Ions and Organic Mercuric Compounds.

By S. AŠPERGER and D. PAVLOVIĆ.

[Reprint Order No. 6006.]

The reaction between potassium ferrocyanide and nitrosobenzene is strongly catalysed by mercuric and mercurous ions and organic mercury compounds except those in which mercury is bound with strong covalent bonds. The catalytic effect was followed by spectrophotometric measurements of the extinction of the violet product $[Fe(CN)_5,PhNO]^{3-}$. Catalytic action relates to the dissociation of $[Fe(CN)_6]^{4-}$ to $[Fe(CN)_5]^{3-}$, as does the action of ultraviolet light. The mechanism of catalysis is discussed. Ions of gold and platinum also act as catalysts. The order of action is $Pt^{4+} < Au^{3+} < Hg^{2+} \approx Hg_2^{2+}$, corresponding to their arrangement in the Periodic System. A method for determining traces of mercury in burnt mercury alloys as well as for the identification of small amounts of pharmaceutical mercury preparations is outlined on the basis of catalytic action.

CONTINUING earlier investigations on the kinetics of the decomposition of potassium ferrocyanide in ultraviolet light (Ašperger, *Trans. Faraday Soc.*, 1952, **48**, 617) and on the kinetics of the reaction of potassium ferrocyanide and nitrosobenzene in water (Ašperger, Murati, and Čupahin, *J.*, 1953, 1041), we have studied the catalytic action of mercuric and mercurous ions and of some organic mercuric compounds on the reaction which proceeds according to equations 1—3. At low concentrations and at room temperature reaction

practically ceases, but in ultraviolet light or on the addition of mercuric ions in a concentration greater than 2×10^{-7}M the violet reaction product is formed.

$$[Fe(CN)_6]^{4-} \overset{H_2O}{\rightleftharpoons} [Fe(CN)_5,H_2O]^{3-} + CN^- \quad . . . . . (1)$$

$$[Fe(CN)_5,H_2O]^{3-} + PhNO \longrightarrow [Fe(CN)_5,PhNO]^{3-} + H_2O \quad . . . . . (2)$$

$$CN^- + H_2O \rightleftharpoons HCN + OH^- \quad . . . . . (3)$$

The kinetics of this reaction are easily studied by spectrophotometric determination of the violet complex. Our previous kinetic measurements largely had the practical purpose of determination of traces of mercuric ions in distilled bromine and chlorine water and of small amounts of mercury vapours in the atmosphere (Ašperger and Murati, *Analyt. Chem.*, 1954, **26**, 543). In the present work we studied the nature of the catalytic action itself.

Experimental

Materials.—Aqueous solutions of nitrosobenzene were prepared as described previously (*locc. cit.*). Molar concentrations given refer throughout to the monomeric form. The solutions of catalysts were prepared by dilution of more concentrated solutions immediately before measurement in order to avoid the influence of adsorption on glass. Jena or Pyrex glassware was used. Potassium ferrocyanide trihydrate and all inorganic mercury compounds were of analytical grade.

Apparatus.—A Unicam S.P. 500 quartz spectrophotometer was used for the spectrophotometric measurements (slit width: 0·01—0·02 mm.; corresponding spectral band width 12—18 Å; 10-mm. glass cells). The extinction was measured at 528 mμ, *i.e.*, at the absorption maximum of $[Fe(CN)_5,PhNO]^{3-}$, which is attributable solely to the violet complex: absorption of other components at 528 mμ is negligible (*J.*, 1953, 1042). Further, allowance was made for any possible influence by other components by use of controls.

Concentrations of Reagents.—If not otherwise indicated, potassium ferrocyanide was $5{\cdot}0 \times 10^{-4}$M and nitrosobenzene $4{\cdot}2 \times 10^{-4}$M. At these concentrations the control solutions, not containing catalyst, are stable for more than 30 min. at 20°. In all cases the extinctions were measured against freshly prepared control solutions.

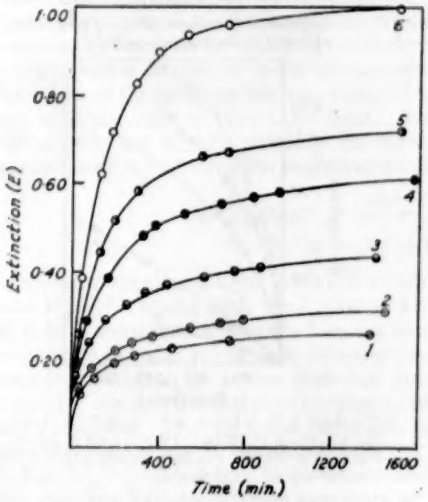
Influence of pH.—The rate of formation of the violet product depends on the pH; it was highest when the pH of the mixture (aqueous nitrosobenzene and catalyst) was adjusted to 3·5 by adding a few drops of hydrochloric acid or potassium hydroxide before the addition of potassium ferrocyanide. (It was erroneously reported in *J.*, 1953, 1043, line 35, that the solution of potassium ferrocyanide was also adjusted to pH 3·5.) When potassium ferrocyanide was added in such an amount that its concentration in the final mixture was 5×10^{-4}M, it caused an increase of the pH from 3·5 to 4·1. Consequently the pH of all our solutions at zero time was 4·1.

Reaction catalysed by Mercuric Ions.—An aqueous solution of nitrosobenzene was prepared, a definite amount of mercuric chloride added, and the pH adjusted to 4·1. The pH of the solution of potassium ferrocyanide was also adjusted to 4·1. These solutions were mixed after thermal equilibrium had been reached at 20°. In the final mixture nitrosobenzene was $1{\cdot}05 \times 10^{-3}$M and mercuric chloride 1×10^{-6}M; the concentration of potassium ferrocyanide varied from $7{\cdot}5 \times 10^{-4}$ to 3×10^{-3}M. At intervals a portion of the solution was drawn off and the extinction measured at 528 mμ. Since in this series of measurements the concentration of potassium ferrocyanide varied, causing changes in the pH of the final mixture, it was necessary to adjust the pH of the solution of potassium ferrocyanide to 4·1. The results, given in Figs. 1 and 2, show that the velocity depends to a great extent on the concentration of potassium ferrocyanide. If reaction (1) is taken as the rate-determining stage, the velocity of formation of the violet product should not be influenced by variations in the initial concentration of nitrosobenzene above a certain point: Fig. 3 shows that this is so for a concentration of nitrosobenzene above 2×10^{-4}M.

Reaction (2), *i.e.*, the reaction between aquopentacyanide and nitrosobenzene, is much faster than reaction (1). Moreover reaction (2) is practically irreversible. If, for example, a mixture of ferrocyanide and nitrosobenzene is first exposed to ultraviolet light and then put in the dark, the extinction of the violet complex remains practically unchanged. On the other hand, reaction (1), *i.e.*, the dissociation of ferrocyanide into aquopentacyanide in the absence of nitrosobenzene, is reversible. The pH of the irradiated ferrocyanide solutions decreases in the dark until the initial pH value is almost regained.

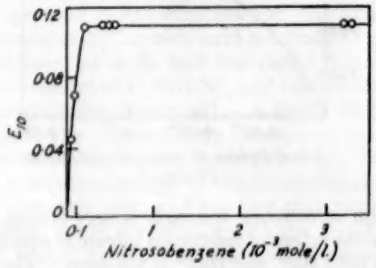
Influence of Temperature.—In the first series of measurements the concentration of mercuric ions was 2×10^{-6}M (Fig. 4), in the second 7×10^{-6}M. If the logarithms of the initial reaction velocity are plotted against $1/T$, a straight line is obtained in each series (Fig. 5). The initial velocity was taken as the height of the ordinate at the intersection of the tangent to the curves

FIG. 1. *Dependence of the reaction velocity on the concentration* (M) *of potassium ferrocyanide.*



$K_4Fe(CN)_6$: 1, $7{\cdot}5 \times 10^{-5}$; 2, 1×10^{-4}; 3, $2{\cdot}5 \times 10^{-4}$; 4, 5×10^{-4}; 5, 1×10^{-3}; 6, 3×10^{-3}M; PhNO $1{\cdot}05 \times 10^{-3}$M; $HgCl_2$ 1×10^{-6}M; *initial* pH = 4·3; $t = 20°$; $\lambda = 528$ mμ.

FIG. 3. *Dependence of initial reaction velocity (E_{10} = extinction at 10 minutes) on concentration of nitrosobenzene.*



$K_4Fe(CN)_6$ 5×10^{-4}M; $HgCl_2$ 7×10^{-6}M; $t = 20°$; *initial* pH = 4·1; $\lambda = 528$ mμ.

FIG. 2. *Dependence of the initial reaction velocity (E_{20} = extinction at 20 minutes) on the concentration of potassium ferrocyanide.*

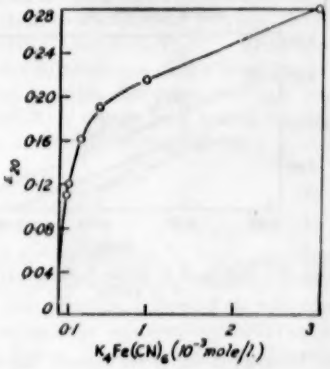
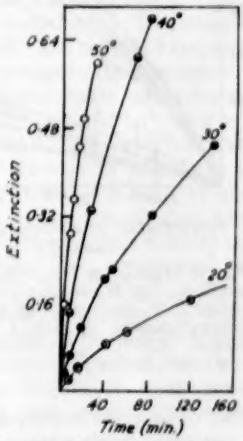


FIG. 4. *Influence of temperature on the velocity of reaction.*



$K_4Fe(CN)_6$ 5×10^{-4}M; PhNO $8{\cdot}38 \times 10^{-4}$M; $HgCl_2$ 2×10^{-6}M; *initial* pH = 4·1; $\lambda = 528$ mμ.

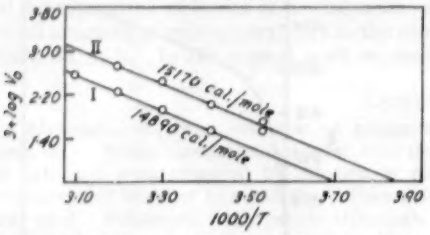
in Fig. 4 at $t = 0$, and the ordinate at $t = 10$. The constants of the straight lines were calculated by the least-squares method. The mean value of the activation energy (15 kcal./mole) is only approximate since, instead of rate constants, the initial velocities were used. The activation energy obtained relates to the slowest process, *i.e.*, the dissociation of $[Fe(CN)_6]^{4-}$ into $[Fe(CN)_5]^{3-}$; it is about 5 kcal./mole lower than that of the uncatalysed process (*J.*, 1953, 1044).

Salt Effect.—The velocity of the catalysed reaction decreases with the increase of ionic strength; *e.g.*, Fig. 6 shows the action of potassium chloride. The negative salt effect is in

agreement with Brönsted's theory, since the charges of ferrocyanide and mercuric ions are of opposite signs.

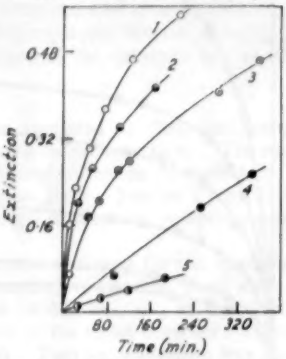
Catalytic Action of Different Mercury Compounds.—The dependence of catalytic action on the concentration of different mercury compounds is shown in Fig. 7. Extinction at 30 min. was taken as a measure of the catalytic action. It can be seen that the catalytic effects of mercuric chloride and bromide are equal; those of mercuric sulphate and nitrate are smaller. This can be ascribed to the salt effect since, in the preparation of the solutions of sulphate and nitrate, acid

FIG. 5. *Influence of temperature on the initial reaction velocity (v_0).*



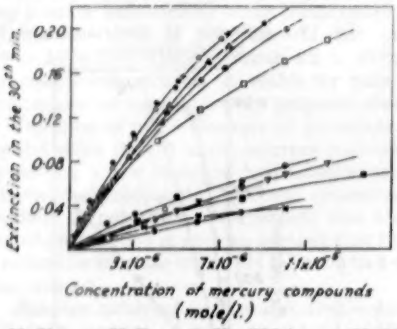
Series I: $HgCl_2$ 2×10^{-4}M. *Series II*: $HgCl_2$ 7×10^{-6}M.

FIG. 6. *Influence of concentration of potassium chloride on the reaction velocity.*



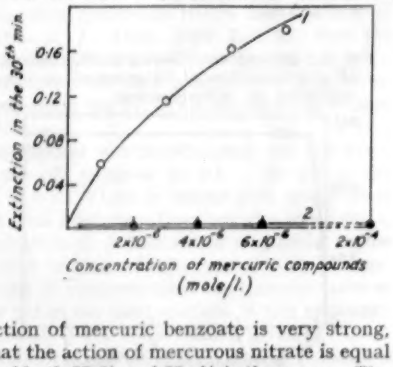
KCl: 1, 0·0; 2, 0·1; 3, 0·3; 4, 0·7; 5, 1·0M; $K_4Fe(CN)_6$ 5×10^{-4}M; PhNO $1·05 \times 10^{-3}$M; $HgCl_2$ 1×10^{-6}M; $t = 20°$; *initial* pH = 4·1; $\lambda = 528$ μm.

FIG. 7. *Dependence of the reaction velocity on the concentration of some mercury compounds.*



○ $HgCl_2$, × $HgBr_2$, ● $Hg_2(NO_3)_2$, △ $HgSO_4$, ◐ $Hg(OBz)_2$, ⓘ $Hg(NO_3)_2$, □ $Hg(CN)_2$, ◒ Ph·Hg·OAc, ▽ Me·HgBr, ■ mercuri-*o*- and -*m*-hydroxybenzoate, ◑ MeHgI, ✱ mercuribis-succinimide. $K_4Fe(CN)_6$ 5×10^{-4}M; PhNO $4·2 \times 10^{-4}$M; $t = 20°$; *initial* pH = 4·1; $\lambda = 528$ mμ.

FIG. 8. *Catalytic action of mercuric chloride (curve 1) and diphenylmercury (curve 2) on the reaction velocity in 73·2% (vol.) methanol.*



was added to suppress hydrolysis. The catalytic action of mercuric benzoate is very strong, that of mercuric cyanide weaker. It is interesting that the action of mercurous nitrate is equal to that of mercuric chloride, *i.e.*, the catalytic action of both Hg^{2+} and Hg_2^{2+} is the same. The effect of phenylmercuric acetate, methylmercuric bromide, mercuri-*o*- and -*m*-hydroxybenzoate $\left(HO{\cdot}C_6H_3\langle^{Hg}_{CO_2}\right]\right)$, methylmercuric iodide, and mercuribis-succinimide $[Hg(N{\cdot}C_4H_4O_2)]$ is much smaller. This is consistent with the view that the catalysis is due to mercuric or mercurous ions for in all these compounds one or both of the mercury bonds are more or less covalent. Diphenylmercury was not expected to exhibit any catalytic action. Since this compound is insoluble in water, alcoholic solutions were prepared containing 73·2% (vol.) of methanol. Under the same conditions measurements were carried out with mercuric chloride. From Fig. 8 it may be seen that diphenylmercury has no catalytic action, even at a concentration 2×10^{-4}M, 100 times greater than the mean concentrations of mercuric chloride used.

Discussion

Reaction between ferrocyanide and nitrosobenzene takes place much faster in ultraviolet light than in the dark; thus we can talk of the catalytic action of light. Our earlier spectrophotometric measurements (*J.*, 1953, 1042) have shown that the same violet product is formed regardless of whether the reaction is catalysed by ultraviolet light or by mercuric ions. The light energy of wavelengths shorter than 400 mμ causes the dissociation of one cyanide group from the hexacyanide ion and accelerates the otherwise very slow thermal reaction. The catalytic action of mercuric ions must relate to the slowest process, shown in the previous section to be the decomposition of $[Fe(CN)_6]^{-4}$ to $[Fe(CN)_5]^{3-}$. Moreover, the action of the mercuric ion was expected to relate to the dissociation of the ferrocyanide ion, as in the case of ultraviolet light. The product of reaction between mercuric and ferrocyanide ion is very probably the intermediate $Hg(CN)^+$, which in a relatively fast reaction with a hydrogen ion regenerates a mercuric ion according to the scheme:

$$Hg^{2+} + [Fe(CN)_6]^{4-} \xrightarrow{H_2O} [Fe(CN)_5,H_2O]^{3-} + Hg(CN)^+ \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$Hg(CN)^+ + H^+ \longrightarrow Hg^{2+} + HCN \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

By this mechanism catalytic action of mercuric ions will not be possible in basic solutions since $Hg(CN)^+$ reacts with the hydroxyl ion, giving $Hg(CN)\cdot OH$ (Borelli, *Gazzetta*, 1908, **38**, I, 361) and mercuric ions are then not regenerated. The catalytic action of all mercuric compounds in basic solutions is actually very small. In an acid solution regeneration is possible and catalytic action does not cease [Pinter, *Farm. Vjesnik*, 1940, **3** (Zagreb, Croatia)]. In fact the action of hydrogen ions is more complicated than might be expected from equation (5). In acid solutions of potassium ferrocyanide we have the following equilibria: $H^+ + [Fe(CN)_6]^{4-} \rightleftharpoons [HFe(CN)_6]^{3-}$ and $H^+ + [HFe(CN)_6]^{3-} \rightleftharpoons [H_2Fe(CN)_6]^{2-}$. According to Nekrasov and Zotov (*J. Appl. Chem. U.S.S.R.*, 1941, **14**, 264), the first two dissociation constants of $H_4Fe(CN)_6$ are very large. The dissociation constants of the third and fourth stages are approximately 10^{-3} and 5×10^{-5} respectively. Assuming the first two dissociations to be complete, we can compute the concentration of ions present in a solution of potassium ferrocyanide. The approximate concentrations of ions in 5×10^{-4}M-potassium ferrocyanide at pH 4·1 are: $[Fe(CN)_6]^{4-}$ $1{\cdot}8 \times 10^{-4}$, $[HFe(CN)_6]^{3-}$ $2{\cdot}9 \times 10^{-4}$, $[H_2Fe(CN)_6]^{2-}$ $2{\cdot}3 \times 10^{-5}$; and at pH 2: $2{\cdot}3 \times 10^{-7}$, $4{\cdot}5 \times 10^{-5}$, and $4{\cdot}5 \times 10^{-4}$ respectively. We see that, in fairly acid solutions of potassium ferrocyanide, $[H_2Fe(CN)_6]^{2-}$ predominates. It might be expected that the smaller the number of protons in the complex ion, the easier would be the loss of the cyanide ions from it. Consequently, in very acid solutions of potassium ferrocyanide the reaction velocity should decrease, as is in fact the case. The two effects of hydrogen ions, suppression of the dissociation of $H_4Fe(CN)_6$ and regeneration of the catalyst, are in opposition, and this must lead to an optimum pH. Actually the maximum reaction velocity is observed when the pH of the final reaction mixture at zero time is 4·1, or the pH of the reaction mixture before adding ferrocyanide is 3·5 (*J.*, 1953, 1041). The negative salt effect, the decrease in activation energy of the decomposition of $[Fe(CN)_6]^{4-}$ into $[Fe(CN)_5]^{3-}$ in the presence of mercuric ions, and the fact that purely covalently bonded mercury gives no catalytic action, are in accordance with the above *general* scheme.

It may be expected that ions of some other heavy metals, which have a close affinity for the cyanide ion and can be regenerated in acid solutions, will also exhibit catalytic action. Gold and platinum ions show catalytic action; on the other hand, none was observed for silver. The increasing order of catalytic action corresponds to the arrangement of these metals in Periodic Table, $Pt^{4+} < Au^{3+} < Hg^{2+} \simeq Hg_2^{2+}$.

Further Use of the Reaction in Analysis.—A method for the determination of small amounts of mercury in burnt mercury alloys remaining in the smelting plants of mercury mines has been developed. About 1 g. of the alloy was heated in an air-stream at 1100°. The mercury vapour liberated was mixed with bromine vapour according to Moldawskii (*J. Appl. Chem. U.S.S.R.*, 1930, **3**, 955; cf. Stock, *Ber.*, 1938, **71**, 550). The mercuric bromide remains in the absorption vessel. The determination of these small amounts of mercuric bromide was performed

according to our earlier procedure (*loc. cit.*, 1954), 23 samples containing 0·002—0·007% of mercury being analysed. The error was about 5%.

Pharmaceutical preparations containing ionic mercury could be identified as mercury compounds even in extremely small quantities. Determination is also possible on the basis of a calibration curve.

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Ultraviolet Absorption Spectra of Some Mercury Compounds.

By B. G. GOWENLOCK and J. TROTMAN.

[Reprint Order No. 6022.]

The absorption spectra of ethanol solutions of some inorganic mercury compounds and of some methyl- and phenyl-mercury derivatives have been measured. The results are discussed in terms of the absorption due to the metal and displacement of the high-intensity absorption band in phenyl and phenylmercury derivatives.

As part of a fundamental study of organomercury compounds, it was decided to measure the ultraviolet absorption spectra of phenylmercury derivatives in dilute solution. The data available (Purvis and McClelland, *J.*, 1912, **101**, 1514) were suspect, the results implying that the well-known phenyl absorption bands were absent in diphenylmercury. Mann, Millar, and Smith (*J.*, 1953, 1130) have shown that Purvis and McClelland's data for triphenylarsine are unreliable. A preliminary notice of our work appeared (*Chem. and Ind.*, 1954, 309) before the publication by Leandri and Tundo (*J.*, 1954, 3377) of a discussion of the absorption spectra of some phenyl-, thienyl-, and furyl-mercury derivatives, the results having previously been published elsewhere (*Boll. Sci. Fac. Chim. Ind. Bologna*, 1952, **10**, 160). The work presented here overlaps, in some measure, that of Leandri and Tundo, their data being confirmed; however, we investigated absorption over a wider range than these authors and studied many other mercury compounds.

Absorption maxima in the region 206—214 mμ are common to all the mercury compounds studied, and it therefore seems probable that this absorption is due to the electrons of the covalently bonded mercury. For phenylmercury derivatives the increased intensity of the absorption in this region relative to that for inorganic and methyl compounds of mercury is probably caused by a combination of the absorption due to the mercury and the undisplaced high-intensity absorption of the phenyl group. Our results are presented in five groups, each containing comparable compounds.

The data for mercuric bromide and iodide (Table 1) are in fair agreement with the values of Butkow (*Z. Physik*, 1931, **71**, 678), who gives $\lambda_{max.}$ 233 mμ ($HgBr_2$), 217 and 272 mμ (HgI_2), and of Scheibe (*Z. Elektrochem.*, 1928, **34**, 497), who gives $\lambda_{max.}$ 210 and 270 mμ (HgI_2). Addition of excess of ammonia to the solutions of the mercuric halides did not alter the absorption, and hence it can be concluded that co-ordination by ammonia has no

TABLE 1. *Inorganic mercury compounds* (see Fig. 1).*

Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
$HgCl_2$	211	3·60	—	— (*a*)	HgI_2	215	4·36	273	3·74 (*b*)
$HgBr_2$	206	3·79	234	3·64 (*b*)	$2HgCl_2,Et_2S$	209	4·02	—	— (*c*)

* In every case data are for ethanol solutions; letters in parentheses refer to preparations.
(*a*) Mersey Chemicals Ltd. (*b*) B.D.H. (*c*) Faragher, Morell, and Comay, *J. Amer. Chem. Soc.*, 1929, **51**, 2774, and McAllan, Cullum, Dean, and Fidler, *ibid.*, 1951, **73**, 3627.

effect on the electronic transitions responsible for the absorption. A similar conclusion is probable for the diethyl sulphide complex which gives an extinction coefficient equal to twice the value for mercuric chloride plus that for diethyl sulphide with an almost unaltered $\lambda_{max.}$ (Et_2S, $\lambda_{max.}$ 210 mμ, log ε 3·25; Fehnel and Carmack, *J. Amer. Chem. Soc.*, 1949, **71**,

84). Confirmation of the ascription of the 206—214 mμ peak to mercury is provided by the fact that other inorganic compounds of mercury absorb in this range: mercurous sulphate, $\lambda_{max.}$ 214 mμ (Kato, *Bull. Inst. Phys. Chem. Res. Japan*, 1930, **12**, 230); mercurous perchlorate, $\lambda_{max.}$ 209 mμ (Higginson, *J.*, 1951, 1438); mercuric and mercurous acetate, $\lambda_{max.}$ 212 mμ; mercuric cyanide, $\lambda_{max.}$ 206 mμ (Gowenlock and Trotman, unpublished data).

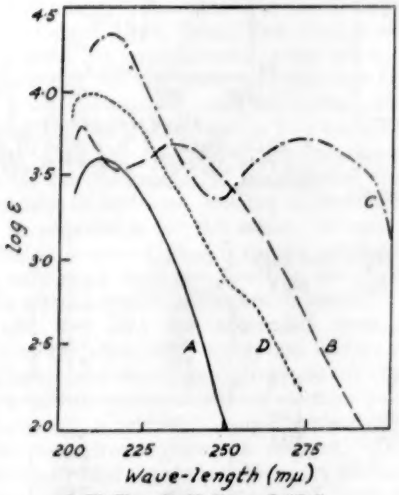
Addition of ammonia to the methyl compounds (Table 2) produces no alteration in the absorption. Methyl-, ethyl-, and *n*-propyl-mercury halides form co-ordination compounds with ammonia (Gowenlock, unpublished data) and it is again apparent that co-ordination has little effect upon the electronic transitions responsible for the absorption. An attempt

TABLE 2. *Alkylmercury halides* (see Fig. 2).

Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
MeHgCl	206	3·17	—	— (*a*)
MeHgBr	209—210	3·54	—	— (*a*)
MeHgI	206	3·89	230	3·60 (*b*)
trans-CHCl:CH·HgCl	212	3·80	—	— (*c*)

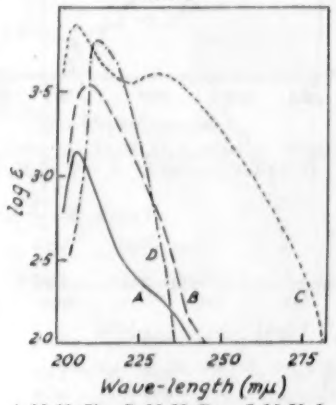
(*a*) Hartley, Pritchard, and Skinner, *Trans. Faraday Soc.*, 1950, **46**, 1019. (*b*) Frankland, *Annalen*, 1853, **85**, 363. (*c*) Friedlina and Nesmeyanov, *Compt. rend. Acad. Sci. U.R.S.S.*, 1940, **26**, 60.

FIG. 1.



A, $HgCl_2$. *B*, $HgBr_2$. *C*, HgI_2. *D*, $2HgCl_2,(C_2H_5)_2S$.

FIG. 2.



A, MeHgCl. *B*, MeHgBr. *C*, MeHgI. *D*, *trans*-Cl·CH:CH·HgCl.

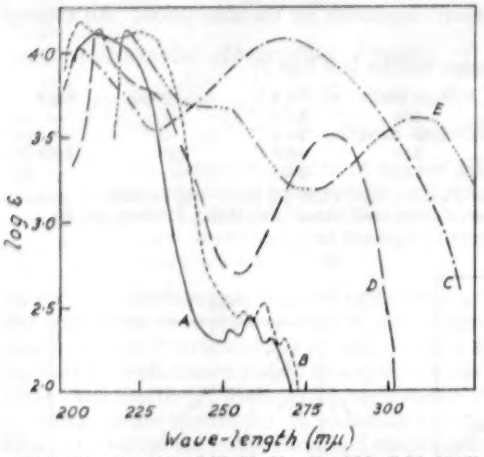
to measure the absorption spectrum of bismethylmercury sulphate indicated a maximum at about 205—207 mμ, but accurate results are not possible owing to the very low solubility of this substance in ethanol.

As mercuric bromide and iodide possess two absorption maxima, aromatic derivatives of ·HgCl alone have been investigated so as to obviate the possibility of other absorptions interfering with the characteristic benzenoid absorption (see Table 3).

Data for X = H, Me, NO_2, and NH_2 have been given by Leandri and Tundo (*loc. cit.*) and are in good agreement with ours in the range 220—300 mμ. (For X = NO_2 their value for log ε should read 4·08 instead of 4·68.) It is well known that substitution in the benzene ring produces bathochromic shifts both in the low-intensity bands, designated *B* bands (Bowden and Braude, *J.*, 1952, 1068) and B_{2u} bands (Craig, *Discuss. Faraday Soc.*, 1950, **9**, 5; Leandri and Tundo, *loc. cit.*), and in the high-intensity bands, designated *E* bands (Bowden and Braude, *loc. cit.*), E_{1u} bands (Craig, *loc. cit.*), and B_{1u} or E_{2g} bands (Leandri and Tundo, *loc. cit.*). Both our observations and those of Leandri and Tundo indicate

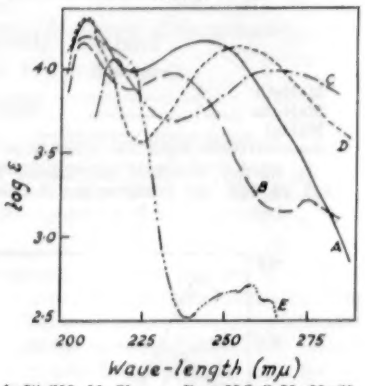
that in some *para*-substituted ·HgCl derivatives, the *B* bands (in Bowden and Braude's terminology) are merged in the displaced *E* bands; discussion is therefore restricted to the high-intensity *E* bands, our data being compared with those for other *para*-disubstituted benzene derivatives (Doub and Vandenbelt, *J. Amer. Chem. Soc.*, 1947, **69**, 2714; Fehnel and Carmack, *ibid.*, 1949, **71**, 2932). Doub and Vandenbelt have shown that in *para*-disubstituted compounds the effect of substituents on the displacement of the *E* band can

FIG. 3.



A, PhHgCl. *B*, *p*-CH_3·C_6H_4·HgCl. *C*, *p*-NO_2·C_6H_4·HgCl. *D*, *o*-HO·C_6H_4·HgCl. *E*, *o*-O^-·C_6H_4·HgCl.

FIG. 4.



A, $PhCH_2$·HgCl. *B*, *p*-HO·C_6H_4·HgCl. *C*, *p*-O^-·C_6H_4·HgCl. *D*, *p*-NH_2·C_6H_4·HgCl. *E*, *p*-NH_3^+·C_6H_4·HgCl.

TABLE 3. *p*-X·C_6H_4·HgCl (see Figs. 3 and 4).

X	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	Ref.
H	211—212	4·10	—	—	252 258 264	2·37 2·46 2·36	(*a*)
Me	206	4·19	224	4·14	256 262 268	2·47 2·53 2·38	(*a*)
NO_2	205	4·02	269	4·09	—	—	(*b*)
NH_2	207	4·29	254	4·14	—	—	(*c*)
NH_2^+	208	4·15	—	—	252 258 264	2·67 2·69 2·60	(*d*)
OH	207	4·15	234	3·97	274—275	3·21	(*e*)
O^-	216 †	4·05	265	4·00	—	—	(*f*)
OH *	212	4·14	225 ‡	3·80	282	3·52	(*e*)
O^- *	220 †	4·15	246 ‡	3·68	309	3·61	(*f*)

(*a*) HgR_2 (B.D.H.) + $HgCl_2$. (*b*) Nesmeyanov, Gluschnev, Epifansky, and Flegontov, *Ber.*, 1934, **67**, 130. (*c*) Dimroth, *Ber.*, 1902, **35**, 2032. (*d*) Addition of HCl to $-NH_2$. (*e*) Whitmore and Middleton, *J. Amer. Chem. Soc.*, 1921, **43**, 619. (*f*) Addition of NaOH to –OH. * *ortho*-Compound. † Absorption due to NaOH masks absorption below 210 mμ. ‡ Inflection.

be correlated with the directive effect of the substituent groups (*i.e.*, *ortho-para-* or *meta*-directing). On this basis, HgCl is essentially similar to Cl, Me, and SMe and different from CO_2H and NO_2. This implies that HgCl is an *ortho-para*-directing group, the effect being weak. A search of the literature suggests that direct experimental evidence is lacking, since most reagents used in substitution in the benzene ring remove the HgCl group from the ring.

A further comparison can be made in the effect of the ionization OH ⟶ O^- on the *E* band for both *para*- and *ortho*-substituted phenols. For the *para*-substituents SMe, Cl, COMe, CHO, and NO_2 the ionization leads to a displacement of $\lambda_{max.}$ to longer wavelengths

by 7, 19, 49·5, 46·5, and 85 mμ, respectively, log ε increasing by amounts varying between 0·12 and 0·29. HgCl similarly displaces $\lambda_{max.}$ to longer wavelengths in this ionization (30 mμ) but in contrast to all the other cases log ε is virtually unaltered. For the *ortho*-

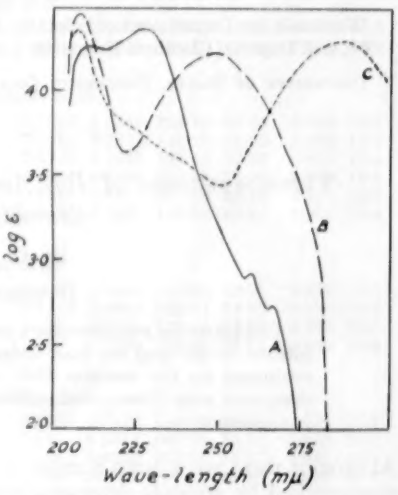
TABLE 4. *Diphenyl compounds* (high-intensity bands only) (see Fig. 5).

Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
Ph_2Hg	209	4·28	226	4·38 (*a*)	Ph_2NH	207—208	4·33	286	4·29 (*a*)
Ph_2CH_2	—	—	220	4·00 (1)	Ph·Ph	207	4·43	248	4·21 (*a*)
$Ph{\cdot}CH_2{\cdot}CH_2Ph$	—	—	219	4·08 (1)	Ph_2S	—	—	250	4·08 (2)

(*a*) Product of B.D.H. Ltd. (1) Braude, *J.*, 1949, 1902. (2) Jaffé, *J. Chem. Phys.*, 1954, **22**, 1430.

substituents SMe, COMe, CHO, NO_2, $CO{\cdot}NH_2$, CN, and CO_2^-, $\lambda_{max.}$ is displaced to longer wavelengths on ionization by the relatively smaller amounts 1, 3·5, 8·5, 3·5, 5·5, 9, and 11·5 mμ, respectively, the log ε alterations being +0·06, −0·28, −0·23, −0·19, −0·04, −0·07, and −0·02. The only substituent giving a comparable displacement to HgCl (21 mμ) is OH (21·5 mμ), log ε alterations being −0·12 and +0·03, respectively. It is apparent that for the groups COMe, CHO, and NO_2 which form strong hydrogen bonds when *ortho* to OH (Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, New York, 1940, p. 318) there is a large decrease in the intensity of absorption for the ionization $OH \longrightarrow O^-$, only when these substituents are in the *ortho*-position, this being accompanied by a markedly smaller shift in the absorption maximum than for the *para*-case. It is suggested that destruction of hydrogen bonding on ionization may be responsible for this effect. If such a conclusion is correct, then it can be concluded that only weak hydrogen bonding can occur within *o*-hydroxyphenylmercuric chloride.

FIG. 5.



A, Ph_2Hg. *B*, Ph·Ph. *C*, Ph_2NH.

Jaffé (*loc. cit.*) has concluded from a study of the ultraviolet absorption spectra of polyphenyl and monophenyl compounds that groups not possessing unshared electron pairs produce only a relatively minor perturbation of the π-electron system in benzene. This would imply that for diphenylmercury and diphenylmethane the transitions in the phenyl groups involve only the electrons of those groups acting independently of one another, whereas in diphenylamine, diphenyl sulphide, and diphenyl these electrons are delocalized over the whole molecule. Inspection of Table 4 confirms Jaffé's conclusions, suggesting that only very weak interaction (presumably through one of the $6p\pi$ or $6d\pi$ orbitals) is possible between the two phenyl groups in diphenylmercury. The marked difference in absorption between diphenylmercury and phenylmercury compounds in the 226 mμ region of the spectrum makes possible a determination of diphenylmercury in the presence of phenylmercury compounds without the use of dithizone (Miller and Polley, *Analyt. Chem.*, 1954, **26**, 1333).

There is a marked difference between the spectrum of benzylmercuric chloride and those of other benzyl compounds (see Table 5). The possibility of dissociative absorption of the

TABLE 5. *Benzyl compounds* (high-intensity bands only).

Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	Compound	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
$Ph{\cdot}CH_2{\cdot}HgCl$...	208	4·29	245	4·16 (*a*)	$Ph{\cdot}CH_3$	209	3·91	—	— (1)
$Ph{\cdot}CH_2Cl$	217	3·85	—	— (*b*)	$Ph{\cdot}C_3H_5$ ...	208	3·89	—	— (2)
$Ph{\cdot}CH_2{\cdot}CH_2Cl$	209	3·87	—	— (*c*)					

(*a*) Hilpert and Gruttner, *Ber.*, 1915, **48**, 913. (*b*) B.D.H. (*c*) Eastman Kodak. (1) Platt and Klevens, *Chem. Reviews*, 1947, **41**, 301. (2) Braude, *loc. cit.*

weak benzyl–mercury bond cannot be ignored, but it was found that absorption did not vary with time. A search of the literature indicates that all other benzyl–X compounds investigated exhibit *B* bands in the region of 250—270 mμ and that any *E* bands are all at lower wavelengths than 230 mμ (X = CO_2H, $CO{\cdot}NH_2$, Guilmart, *Bull. Soc. chim.*, 1938, **5**, 1209; X = OH, CN, Mohler and Polya, *Helv. Chim. Acta*, 1936, **19**, 1222). Comparable data for other benzyl-metal compounds are desirable.

Experimental

All substances, whether obtained commercially or prepared by us (see footnotes to tables), were, where possible, recrystallized from spectroscopic ethanol (Bladon, Henbest, and Wood, *J.*, 1952, 2737) and dried under oil-pump vacuum. Spectra were measured in this solvent, the concentrations being chosen so as to obtain optical densities between 0·3 and 0·6 at the absorption maxima, and a Unicam Spectrophotometer SP 500 with corrected scale and 1-cm. quartz cells being used throughout. Absorption could be studied to about 202 mμ under these conditions. All results could be reproduced accurately, the limits being $\lambda_{max.} \pm 0{\cdot}5$ mμ, $\varepsilon \pm 1\%$.

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University of Wales, University College, Swansea. [*Received, January 10th*, 1955.]

Thermodynamics of Ion Association. Part I. Lead Chloride, Bromide, and Nitrate.

By G. H. Nancollas.

[Reprint Order No. 5886.]

Conductivity measurements are reported for lead chloride, bromide, and nitrate at 25° and for lead bromide at 35°. ΔH, ΔG, and ΔS values are evaluated for the reaction $Pb^{2+} + X^- \rightleftharpoons PbX^+$, the entropy changes are compared with those calculated from an entropy cycle, and their significance is discussed.

Although there are a large number of complex species which have been identified and characterised by accurate determinations of stability constants, there are few for which temperature-coefficient data are available so that heat and entropy values can be calculated. The significance of many of the reported values is doubtful since the authors neglected to take into account variations in activity coefficients when the ionic strength was held constant. Empirical relations have been put forward in an attempt to correlate experimental association constants with properties of the metal ion involved. Such relationships, however, are of limited applicability.

The aim of the present work is a systematic study of the thermodynamic properties of ion-association reactions derived from thermodynamic equilibrium constants. This will enable more extensive correlations to be made than have hitherto been possible, and it is hoped that such a study will further clarify the factors affecting the values of *K* and provide some additional basis for a better understanding of the theory of ionic interactions in aqueous media.

Experimental

Conductivity measurements were made with a screened a.c. bridge described elsewhere (Jones and Joseph, *J. Amer. Chem. Soc.*, 1928, **50**, 1049; Shedlovsky, *ibid.*, 1930, **52**, 1793). The experimental technique and method of cell calibration have been described by Davies (*J.*, 1937, 432). Conductivity water was prepared by mixed-bed deionisation (Davies and Nancollas, *Chem. and Ind.*, 1950, **7**, 129) on the ion-exchange resins Nalcite SAR and Nalcite HCR: its specific conductivity was usually about $0{\cdot}08 \times 10^{-6}$ ohm^{-1}. During measurements at 35°, a stream of hot air prevented condensation on the cap of the cell.

Lead Nitrate.—The " AnalaR " salt was recrystallised three times from conductivity water and dried at 100—110°.

Lead Chloride.—Conductivity water at 100° was saturated with reagent-grade lead chloride. After filtration, a few drops of hydrochloric acid were added and the crystals formed on cooling were recrystallised three times in the same way. The salt was dried at 110° for 24 hr.

Lead Bromide.—Lead bromide was prepared by adding stoicheiometric proportions of potassium bromide solution to boiling lead nitrate solution. The salt crystallised on cooling and was purified by three recrystallisations from conductivity water. Owing to the well-known difficulty in dissolving lead bromide, stock solutions were filtered before use and analysed gravimetrically (±0·02%) for bromide (Vogel, " A Test-Book of Quantitative Inorganic Analysis," Longmans, Green & Co., 1947, p. 475).

Conductivity figures at 25° and 35° are given in Table 1, in which c = equiv./l.

TABLE 1.

Expt.	10^4M	10^2c	Λ	10^4I	α	K	Expt.	10^4M	10^2c	Δ	10^4I	α	K
Conductivity of lead chloride at 25°													
1	2·2674	2·1295	140·21	6·728	0·984	38·3	2	5·1355	3·2050	136·78	15·05	0·965	40·6
1	3·0901	2·4860	139·12	9·140	0·979	40·1	2	15·162	5·505	130·10	43·15	0·923	38·0
1	4·3976	2·9660	137·41	12·91	0·968	39·8							
Conductivity of lead nitrate at 25°													
1	1·6163	1·7979	137·88	4·836	0·996	13·8	3	5·6395	3·3584	133·80	16·74	0·986	15·2
2	2·2514	2·1220	136·63	6·727	0·994	15·2	1	7·2992	3·8205	132·72	21·63	0·982	15·5
1	3·0988	2·4890	136·04	9·246	0·992	14·7	2	7·7788	3·9443	132·52	23·36	0·981	15·4
2	3·4628	2·6316	135·62	10·32	0·991	15·2	3	9·1574	4·2796	131·86	27·09	0·979	14·8
1	3·8364	2·7700	135·17	11·43	0·990	15·4	2	9·6221	4·387	131·55	28·42	0·977	15·5
1	4·4267	2·9755	134·74	13·18	0·989	14·9	3	22·617	6·725	126·39	65·82	0·955	15·4
2	4·6816	3·0599	134·51	13·93	0·988	15·3							
Conductivity of lead bromide at 25°													
1	1·5755	1·7751	143·86	4·700	0·992	29·8	2	4·5005	3·0002	140·60	13·31	0·978	29·7
2	1·9019	1·9503	143·40	5·667	0·990	29·7	1	6·3440	3·5620	138·97	18·65	0·970	29·9
1	2·5269	2·2481	142·64	7·517	0·987	29·1	2	8·1250	4·0310	137·54	23·76	0·962	30·5
2	3·4631	2·6317	141·63	10·27	0·983	29·0	1	11·370	4·7700	135·61	32·97	0·950	30·3
1	3·6200	2·6907	141·46	10·73	0·982	29·5							
Conductivity of lead bromide at 35°													
1	2·7053	2·2673	174·09	8·05	0·984	34·3	3	8·5790	4·1422	166·98	24·95	0·954	35·7
2	3·7503	2·7387	172·76	11·11	0·979	33·5	2	10·495	4·5810	165·20	30·31	0·945	35·5
1	4·8218	3·1054	171·36	14·22	0·974	33·1	3	12·560	4·9710	163·31	35·47	0·940	34·5
2	6·2880	3·5463	169·49	18·44	0·965	35·4	3	14·015	5·2940	161·63	40·08	0·930	36·7
1	7·5050	3·8740	168·16	22·52	0·960	34·7							

Results.—Thermodynamic association constants have been obtained from the conductivity data by the method of Righellato and Davies (*Trans. Faraday Soc.*, 1930, **26**, 592) for 2 : 1 and 1 : 2 electrolytes. Mobility terms were evaluated from the empirical equations

$$[\Lambda_{(Pb^{++})} + \Lambda_{(X^-)}] = \Lambda^0 - bf_{(2\text{-}1)}(I)$$
$$[\Lambda_{(PbX^+)} + \Lambda_{(X^-)}] = \Lambda^0 - b'f_{(1\text{-}1)}(I)$$

where b and b' are the respective Onsager slopes, and I is the ionic strength. $f_{(1\text{-}1)}(I)$ values at 25° have been given by Robinson and Davies (*J.*, 1937, 574); $f_{(2\text{-}1)}(I)$ values at this temperature were calculated from the data of Shedlovsky and Brown (*J. Amer. Chem. Soc.*, 1934, **56**, 1069) for calcium and magnesium chlorides, which are assumed to be completely dissociated. At 35°, Gunning and Gordon's data (*J. Chem. Phys.*, 1942, **10**, 126; 1943, **11**, 18) were used to obtain $f_{(1\text{-}1)}$ and in the absence of data for 2 : 1 electrolytes, $[\Lambda_{(Pb^{++})} + \Lambda_{(Br^-)}]$ values were evaluated from Onsager's equation

$$[\Lambda_{(Pb^{++})} + \Lambda_{(Br^-)}] = \Lambda^0 - 188{\cdot}17\sqrt{I}$$

Limiting conductivities were obtained by extrapolating the data by Onsager's method (*Physikal. Z.*, 1927, **28**, 277): at 35°, $\Lambda^0_{PbBr_2} = 181{\cdot}1$. The mobility of the bromide ion being taken as 94·05 (Gunning and Gordon, *loc. cit.*), that of the lead ion is 87·05. At 25°, $\Lambda^0_{Pb^{++}} = 69{\cdot}46$, which compares well with the value, 69·4, obtained by James (*J. Amer. Chem. Soc.*, 1949, **71**, 3243) by re-extrapolating Norman and Garrett's conductivity figures for lead chloride (*ibid.*,

1947, **69**, 110). The mobilities of intermediate ions PbX^+, 45 at 25° and 52 at 35°, were estimated from the value used by Righellato and Davies at 18° (*loc. cit.*).

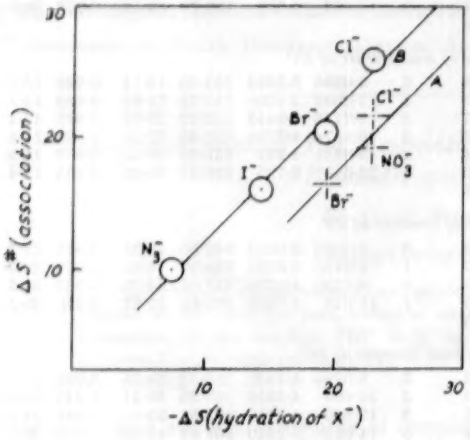
If α is the degree of dissociation and M the molar concentration, the thermodynamic association constant is given by,

$$\log K = \log (1 - \alpha)/\alpha M(1 + \alpha) + 2[I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}2I]$$

and was obtained by successive approximations of I. Values of K are given in Table 1, the mean values being: at 25°, $K_{PbCl^+} = 39{\cdot}2$, $K_{PbBr^+} = 29{\cdot}7$, $K_{PbNO_3^+} = 15{\cdot}1$, and at 35°, $K_{PbBr^+} = 34{\cdot}8$. The figure for lead chloride agrees closely with the value, 38·5, calculated by James (*loc. cit.*).

Discussion

In Table 2 are given ΔH, ΔG, and ΔS values calculated from the K values at 25° and 35° and using the data at 18°, *viz.*, $K_{PbCl^+} = 32{\cdot}9$, $K_{KbNO_3^+} = 15{\cdot}45$ (Righellato and Davies, *loc. cit.*). The Figure suggests that the linear relationship between ΔS(association) and ΔS(hydration) of the anion which was found for other systems (Evans and Nancollas, *Trans. Faraday Soc.*, 1953, **49**, 363) is again obeyed.



Relation between the entropy of association and the entropy of hydration of the anion.
A, PbX^+ (+).
B, $Co(NH_3)_5X^{2+}$ (○).

Table 2. *Thermodynamic properties.*

Reaction	ΔG at 25° (kcal./mole)	ΔH (kcal./mole)	ΔS (expt.) (cal./deg. mole)	ΔS (calc.) (cal./deg. mole)
$Pb^{2+} + Cl^- \rightleftharpoons PbCl^+$	−2·18	4·38	22·0	19
$Pb^{2+} + Br^- \rightleftharpoons PbBr^+$	−2·02	2·88	16·4	15
$Pb^{2+} + NO_3^- \rightleftharpoons PbNO_3^+$	−1·62	−0·57	3·5	5
$Co(NH_3)_5^{3+} + Cl^- \rightleftharpoons Co(NH_3)_5Cl^{2+}$	−3·54	4·32	26	19
$Co(NH_3)_5^{3+} + Br^- \rightleftharpoons Co(NH_3)_5Br^{2+}$	−3·25	2·83	20	14
$Co(NH_3)_5^{3+} + I^- \rightleftharpoons Co(NH_3)_5I^{2+}$	−2·66	2·13	16	10
$Co(NH_3)_5^{3+} + N_3^- \rightleftharpoons Co(NH_3)_5N_3^{2+}$	−2·74	−3·01	−1·0	−6

The entropy of association in aqueous solution, ΔS, may be evaluated from the entropy cycle:

$$\begin{array}{ccc} Pb^{2+}(g) + X^-(g) & \xrightarrow{\Delta S_4} & PbX^+(g) \\ \uparrow \Delta S_1 \quad\quad \uparrow \Delta S_2 & & \downarrow \Delta S_3 \\ Pb^{2+}(aq) + X^-(aq) & \xleftarrow{-\Delta S} & PbX^+(aq) \end{array}$$

where $\Delta S_1 = -\Delta S$(hydration) of gaseous Pb^{2+} ions, $\Delta S_2 = -\Delta S$(hydration) of gaseous X^- ions, $\Delta S_3 = \Delta S$(association) in the gas phase, and $\Delta S_4 = \Delta S$ hydration of the ion-pair.

$$\Delta S = \Delta S_1 + \Delta S_2 + \Delta S_3 + \Delta S_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

ΔS_1 and ΔS_2 were obtained from the known standard and gas-phase entropies (Latimer, "Oxidation Potentials," Prentice-Hall, New York, 1952). ΔS_4 values were estimated by using the empirical equations suggested by Cobble correlating the partial molar entropies of aqueous complex ions as a function of the ratio of their charge to interatomic distance (*J. Chem. Phys.*, **1953**, **21**, **1446**). They are: $\Delta S_4(PbCl^+) = -21{\cdot}5$, $\Delta S_4(PbBr^+) = -20{\cdot}5$, and $\Delta S_4(PbNO_3^+) = -41$ cal./deg. mole.

In calculating ΔS_3, both translational and rotational terms must be taken into consideration,

$$\Delta S_3 = S_{trans}(PbX^+) - S_{trans}(Pb^{2+}) - S_{trans}(X^-) - S_{rot}(X^-) + S_{rot}(PbX^+)$$

The first three terms were obtained from the Sackur–Tetrode equation which for 25° may be written $S_{trans} = 1{\cdot}5\boldsymbol{R} \ln \boldsymbol{M} + 26{\cdot}03$, where M = molecular weight. $S_{rot}(X^-)$, of consequence only in the case where X^- represents the nitrate ion, was calculated from the equation (Herzberg, "Infra-red and Raman Spectra," Van Nostrand, New York, **1945**, Chap. 5) $S_{rot} = 2{\cdot}2868\ (3 \log T + 3 \log I_A) + 264{\cdot}65$, where I_A is the moment of inertia about an N–O bond: $S_{rot}(NO_3^-) = 19{\cdot}4$ cal./deg. mole.

$PbCl^+$ and $PbBr^+$ being treated as simple "dumbell" molecules, their rotational entropies, $S_{rot} = 4{\cdot}606 \log IT + 177{\cdot}7$, where I is the moment of inertia. Additional terms to account for free internal rotation were introduced for $PbNO_3^+$ and it was assumed that its centre of mass lies on the Pb–N axis. This is not likely to introduce serious error since it will in any case lie close to this axis. The sum of the translational and rotational contributions,

$$S_{trans}(PbNO_3^+) + S_{rot}(PbNO_3^+) = 2{\cdot}2868\ (8 \log T + 3 \log M + \log I_A I_B I_C) - 7{\cdot}697$$

The product, $I_A I_B I_C$, of the moments of inertia was evaluated (Wilson, *Chem. Rev.*, **1940**, **27**, 17; Hirschfelder, *J. Chem. Phys.*, **1940**, **8**, 431) by means of

$$I_A I_B I_C = \begin{vmatrix} +I_{xx} & -I_{xy} & -I_{xz} \\ -I_{xy} & +I_{yy} & -I_{yz} \\ -I_{xz} & -I_{yz} & +I_{zz} \end{vmatrix}$$

where I_{xx}, I_{xy} . . . . are the moments and products of inertia with respect to a co-ordinate system having the centre of mass as origin and the Pb–N axis as x axis: $S_{trans}(PbNO_3^+) + S_{rot}(PbNO_3^+) = 69{\cdot}93$ cal./deg. mole. The contribution due to free internal rotation,

$$S_{f.i.r.} = 2{\cdot}2868\ (\log T + \log I_r - 0{\cdot}602) + 89{\cdot}93$$

where I_r, the "reduced" moment of inertia, is given (Herzberg, *op. cit.*) by

$$I_r = I^0_r[1 - I^0_r(\lambda_{rA}^2/I_A + \lambda_{rB}^2/I_B)]$$

In this formula, I^0_r is the moment of inertia of the "NO_2 top," and λ_{rA} and λ_{rB} are direction cosines: $S_{f.i.r.}(PbNO_3^+) = 5{\cdot}9$ cal./deg. mole.

Substitution in equation (1) of these calculated entropies enables ΔS(association) to be determined. Table 2 shows the good agreement with the experimental values. In the figure, the value of ΔS(association) ($PbNO_3^+$) is corrected for that part of the rotational entropy of the NO_3^- ion which is destroyed in the course of the reaction.

Many of the reported values for the heats and entropies of complex formation are subject to large errors inherent in the conditions for their study (*i.e.*, high ionic strength). Too little is known of the variation of activity coefficients at constant ionic strength to permit reliable estimates of the uncertainties from this source. Stability constants so obtained, although internally consistent, are inconsistent with data at other values of I. For this reason, the results of previous work on the association of hexamminocobalt with halide and azide ions (Evans and Nancollas, *loc. cit.*) have been corrected by multiplying the association constants by $f_{Co(NH_3)_6X^{2+}}(f_{Co(NH_3)_6^{3+}} \cdot f_{X^-})^{-1}$, the activity coefficients being calculated from the Debye–Hückel equation, $-\log f_i = Az_i^2 I^{\frac{1}{2}}$. Thermodynamic properties are included in Table 2 and plotted in the figure. Despite the difference

in absolute values, it is seen that the same linear relation is obeyed both with uncorrected and with corrected constants. The difference between the parallel straight lines may be expressed as

$$[\Delta S_1(Co(NH_3)_6^{3+}) - \Delta S_4(Co(NH_3)_6X^{2+})] - [\Delta S_1(Pb^{2+}) - \Delta S_4(PbX^{+})]$$

This is about 2·5 cal./deg. mole, which may be compared with the observed difference, 4 cal./deg. mole. The discrepancy between ΔS(expt.) and ΔS(calc.) for the hexammino-cobalt system is probably due to the difficulty in obtaining a reliable estimate for the hydration entropy of a tervalent cation.

It has been suggested (Bernal and Fowler, *J. Chem. Phys.*, 1933, **1**, 515) that ions in aqueous solution order the water molecules around them. The removal of ions from solution accompanying complex formation will lead to a breakdown of this order resulting in an entropy change favouring complex formation. The results of the present work are in support of this, the entropy of association being closely related to the entropy of hydration of the anion. A similar comparison should be possible for the formation of complexes of different cations with the same anion, and in this case, the hydration entropy of the cation should be the controlling factor.

To explain the heat changes upon complex formation, three factors must be taken into consideration: electrostatic and covalent interactions, and additional stabilization due to the different available bonding orbitals of the cation (Williams, *J. Phys. Chem.*, 1954, **58**, 121). For bivalent ions of very similar radius, ΔH would be dependent upon the ionization potential of the cation, and if the entropy of association is assumed to be constant, this leads to the linear relationship between log K and ionization potential which is obeyed approximately for closely related cations (*e.g.*, Calvin and Melchior, *J. Amer. Chem. Soc.*, 1948, **70**, 3270; Evans and Monk, *J.*, 1954, 550). More extensive correlations might well be fortuitous until more accurate entropy data are available.

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Reaction of 1 : 2 : 3 : 6-*Tetrahydrobenzaldehyde with Alkali.**

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The reaction of 1 : 2 : 3 : 6-tetrahydrobenzaldehyde with alkali has been studied. With increasing temperature these reactants provide (*a*) a trimer, (*b*) a glycol and the tetrahydrobenzoic acid, (*c*) the tetrahydrobenzyl alcohol and Δ^3-tetrahydrobenzoic acid, and (*d*) pimelic acid and a mixture of hydrocarbons. Good yields of the alcohol and acid are obtained by the Tischtschenko reaction.

WERBER, JANSEN, AND GRESHAM (*J. Amer. Chem. Soc.*, 1952, **74**, 532) found that, although 1 : 2 : 3 : 6-tetrahydrobenzoic acid and alkali gave pimelic acid in high yield (78%), the corresponding aldehyde, with alkali at 350°, gave a low yield of pimelic acid (42%) together with much hydrocarbon (mainly toluene). Our results with the aldehyde agree with those of the American workers provided that high temperatures and concentrated alkali are employed: 48—50% yields of pimelic acid were obtained by use of a 50% excess of 40% aqueous sodium hydroxide at 300—350°. Reduction in the quantity or the concentration of alkali lowered the yield, but variation in time of heating (3—6 hr.) produced little effect. Potassium hydroxide could successfully replace sodium hydroxide, but not calcium hydroxide, sodium carbonate, or trisodium phosphate with which the only products isolated were 1 : 2 : 3 : 6-tetrahydro-benzyl alcohol and -benzoic acid and high-boiling gums. The aldehyde may be replaced by its solid trimer (produced by the action of acid; Chayanov, *J. Gen. Chem. U.S.S.R.*, 1938, **8**, 460): the acid products from this reaction

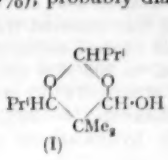
* This work is the subject of B.P. 679,854, 710,002, 711,424, 713,639, and U.S.P. 2,673,219, 2,698,339.

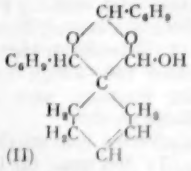
contained, in addition to pimelic acid, 1 : 2 : 3 : 6- and 2 : 3 : 4 : 5-tetrahydrobenzoic and hexahydrobenzoic acid; the neutral products were largely hydrocarbons, boiling over a wide range, and contained toluene, 1-methyl*cyclo*hexene, conjugated dienes, and some 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol and gum.

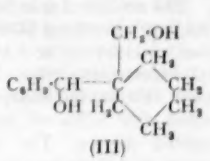
In view of the complexity of the products the reaction was studied in stages. The aldehyde with 30—40% alkali at <60° led to mainly a high-boiling, viscous syrup, and traces of tetrahydro-benzyl alcohol and -benzoic acid. This syrup was not the aldol: the molecular weight indicated a trimer and, by comparison with the trimeric product (I) of reaction of *iso*butyraldehyde with alkali (Saunders, Murray, and Cleveland, *J. Amer. Chem. Soc.*, 1943, **65**, 1714; Villani and Nord, *ibid.*, 1946, **68**, 1674; Alexander and Marvel, *ibid.*, 1950, **72**, 1396), it seemed probable that the main product here was the trimer (II).

The trimer from *iso*butyraldehyde yielded a glycol, $CHMe_2 \cdot CH(OH) \cdot CMe_2 \cdot CH_2 \cdot OH$, and *iso*butyric acid when boiled with alcoholic alkali; the trimer, supposedly (II), with boiling, concentrated, aqueous alkali was completely converted into 1 : 2 : 3 : 6-tetrahydrobenzoic acid (1 mol.) and a glycol (1 mol.), which, by analogy with the glycol from (I), is probably (III). The aldehyde under similar conditions provided the glycol (III) and acid directly: use of more dilute sodium hydroxide led to incomplete conversion into acid and glycol (cf. Table 4). Further attempts to form the aldol failed, including reaction of the aldehyde with cold alcoholic sodium hydroxide (Celanese Corp., U.S.P. 2,436,416, 2,450,498; B.P. 587,749) and with 10% aqueous potassium hydroxide at −20° in the presence of di-*n*-butylamine. The latter experiment yielded only the solid aldehyde hydrate. Hence the aldol is probably unstable or produced under very limited conditions.

The glycol, supposedly (III), consisted of a mixture of solid (*ca.* 67%) and liquid (*ca.* 33%), probably diastereoisomers.


(I)

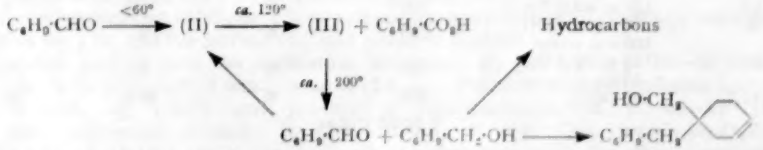

(II)


(III)

(C_6H_9 = *cyclo*hex-3-enyl)

Further reaction of the glycol and alkali at *ca.* 200° gave mainly 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol and -benzoic acid, with a higher-boiling alcohol (probably a Guerbet self-condensation product of the tetrahydrobenzyl alcohol) and much residue. With sodium carbonate there was incomplete reaction.

Thus the overall reaction is of the Cannizzaro type, and it has recently been found that such reactions take place at 200° with aldehydes which give other products at lower temperatures (Hausermann, *Helv. Chim. Acta*, 1951, **34**, 1211). The glycol (III) probably decomposes *via* alcohol and aldehyde (cf. the decomposition of αα-dialkyl-β-hydroxy-acids; Asselineau and Lederer, *Nature*, 1950, **166**, 783), and the probable complete reaction sequence is as annexed.



French and Gallagher (*J. Amer. Chem. Soc.*, 1942, **64**, 1497) stated that aldehydes of similar type underwent a Cannizzaro reaction when treated in methanol with concentrated aqueous potassium hydroxide, but it was found that under these conditions, although the corresponding acid was formed in reasonable yield, the neutral product consisted of the glycol (III) with only a little of the alcohol. Use of aqueous sodium hydroxide and methanolic sodium methoxide led to similar results.

The highest yields of tetrahydro-benzyl alcohol and -benzoic acid were obtained by hydrolysis of the ester obtained from the aldehyde by the Tischtschenko reaction; the anhydrous aldehyde gave 90—95% of tetrahydrobenzyl tetrahydrobenzoate without use of a solvent. Traces of acid (even ½% formed by autoxidation) in the aldehyde were found to inhibit this condensation, as also did higher temperatures.

The reaction of concentrated alkali at 300—350° with compounds related to the aldehyde was briefly studied (cf. Table 1). The neutral products from the tetrahydro-

TABLE 1.

Starting material	Pimelic acid (%)	Starting material	Pimelic acid (%)
Aldehyde diethyl acetal	3—4	Trimer (II)	48
Aldehyde–ammonia complex	10—15	1 : 2 : 3 : 6-Tetrahydrobenzyl alcohol	7
Aldoxime	*ca.* 90	1 : 2 : 3 : 6-Tetrahydrobenzoic acid	85—90
Glycol (III)	*ca.* 25		

benzyl alcohol were hydrocarbons, as in the reaction of the aldehyde and alkali at 300—350°, and it is evident that these were derived from the alcoholic portion in the above reaction sequence; dehydration followed by hydrogenation–dehydrogenation and polymerisation must be involved in this degradation.

EXPERIMENTAL

The 1 : 2 : 3 : 6-tetrahydrobenzaldehyde, produced by reaction of butadiene and acraldehyde, was refractionated before use and had b. p. 53°/11 mm., n_D^{20} 1·4724.

Reactions of 1 : 2 : 3 : 6-*Tetrahydrobenzaldehyde and Alkali.*—(a) *One-stage reaction at* 250—350°. The results of selected experiments are given in Table 2. The reactions were carried out in a rocking autoclave (450 c.c.; stainless steel), and the pimelic acid was removed from the acidified product by continous extraction with ether. The combined neutral extracts from several experiments were distilled. Fractions boiling from 96°/1 atm. to 200°/0·6 mm. were collected, few having sharp b. p.s: *ca.* 25% boiled in the range 96°/1 atm. to 76°/26 mm. and contained (by infra-red analysis) toluene (60—70%), 1-methyl*cyclo*hexene (15—20%), and conjugated dienes. The higher-boiling fractions were also mainly hydrocarbons (partly aromatic), and there was much undistillable residue.

The combined acid products were converted into ethyl esters, fractionation of which esters gave the following fractions: (1) b. p. 74°/9·5 mm., (2) b. p. 88—90°/10 mm., (3) b. p. 135—137°/10 mm., (4) b. p. 86°/0·5 mm., (5) b. p. 125°/0·5 mm., and (6) b. p. 135—138°/0·5 mm.

TABLE 2.

Reactants				Yield of pimelic acid	
Aldehyde (g.)	NaOH (c.c.)	Temp.	Time (hr.)	Wt. (g.)	%
45	123 (40%)	300°	6	31·5	48·2
59	108 (40%)	300	6	34·5	40·3
53·5	114 (47·8% KOH)	300	6	28·8	37·0
60	164 (15%)	250	24	3·4	3·9
45	123 (40%)	300	3	28·6	43·7
45	164 (30%)	300	6	21·6	33·0
50	75 g. $NaCO_3$ + 115 c.c. water	300	6	0	—
110	120 g. solid NaOH	300	6	8·5	5·3
80	80·8 g. $Ca(OH)_2$ + 100 c.c. water	295	6	0	—
34·5	155 g. Na_3PO_4 + 48·6 c.c. water	295	6	0	—
45 *	123 (40%)	300	6	30·5	46·6

* Solid trimer.

Fraction 1 consisted mainly of ethyl hexahydrobenzoate, hydrolysis yielding slightly impure hexahydrobenzoic acid, m. p. *ca.* 30° [*p-bromophenacyl ester*, m. p. 90—91·5° (Found: C, 55·4; H, 5·45; Br, 24·2. $C_{15}H_{17}O_3Br$ requires C, 55·4; H, 5·2; Br, 24·6%); amide, m. p. 184—185° (Found: C, 66·3; H, 10·1; N, 11·1. Calc. for $C_7H_{13}ON$: C, 66·1; H, 10·2; N, 11·0%); anilide, m. p. 145—146° (Found: C, 76·8; H, 8·2; N, 7·0. Calc. for $C_{13}H_{17}ON$: C, 76·8; H, 8·4; N, 6·9%)].

Fraction 2 consisted mainly of ethyl 2 : 3 : 4 : 5-tetrahydrobenzoate, hydrolysis yielding a

product, b. p. 134°/14 mm. (Found: equiv., 127. Calc. for $C_7H_{10}O_2$: equiv., 126). A small quantity of benzoic acid was removed from a cooled light petroleum solution, and the filtrate, after evaporation, provided the following derivatives of 2 : 3 : 4 : 5-tetrahydrobenzoic acid: *p-bromophenacyl ester*, m. p. 102—103° (Found: C, 55·8; H, 4·8; Br, 24·9. $C_{15}H_{15}O_3Br$ requires C, 55·7; H, 4·6; Br, 24·8%); amide, m. p. 121—123° (Found: C, 67·6; H, 8·3; N, 10·7. Calc. for $C_7H_{11}ON$: C, 67·2; H, 8·8; N, 11·2%); anilide, m. p. 105—107° (Found: C, 76·3; H, 7·25; N, 7·9. Calc. for $C_{13}H_{15}ON$: C, 77·6; H, 7·5; N, 7·0%). Treatment with bromine in chloroform, followed by evaporation, gave 1 : 2-dibromo*cyclo*hexane-1-carboxylic acid, m. p. 144—146° (Found: C, 29·6; H, 3·6; Br, 55·9%; equiv., 280. Calc. for $C_7H_{10}O_2Br_2$: C, 29·4; H, 3·5; Br, 55·9%; equiv., 286). The reported m p.s are 124° and 129—130·5° (amide), 110—111° (anilide), and 147° (dibromo-compound).

Fractions 3 and 4 were practically identical and the physical constants (n_D^{20} 1·4332—1·4360; d_4^{20} 0·991, 0·996) agree with those of diethyl pimelate (b. p. 92—93°/0·7 mm., n_D^{20} 1·4306, d_{20}^{20} 0·994).

Fractions 5 and 6 appeared to be esters of high molecular weight.

Although ethyl 1 : 2 : 3 : 6-tetrahydrobenzoate was not isolated the acid was subsequently found in the products of many experiments.

(b) *Reaction at* <65°. (i) The aldehyde (180 g.) was added gradually, with cooling and stirring, to 40% sodium hydroxide solution (492 c.c.); the highest temperature reached was 60°. The product was diluted and ether-extracted; the extract on distillation provided some unchanged aldehyde (29·4 g., containing a little 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol), a main fraction (125·4 g.; n_D^{20} 1·5311, b. p. 208—214°/0·7 mm.), and residue (14·5 g.). The properties of the main distillate, the trimer (II), are given in Table 3. The compound gave no evidence of the presence of a carbonyl group with hydroxylamine hydrochloride or 2 : 4-dinitrophenylhydrazine hydrochloride. The aqueous alkali solution from the aldehyde–alkali reaction was acidified and continuously extracted with ether; it yielded an oily acid (1 g.; equiv., 148).

(ii) The aldehyde (50 g.) and 4% aqueous sodium hydroxide (250 c.c.), stirred for 5 hr. at room temperature, gave aldehyde (40·5 g.), high-boiling material (1·0 g.), and acid (1·1 g.).

(iii) (cf. Celanese Corp., *loc. cit.*). The aldehyde (300 g.), when stirred with a saturated solution of sodium hydroxide in 95% ethanol at <65°, provided low-boiling products (16·5 g.), trimer, b. p. 195—210°/1·5 mm. (248 g.), and residue (13 g.).

TABLE 3.

	Found	Calc. for: aldol	trimer
M (cryoscopic)	326, 346	220	330
Unsaturation equiv. (hydrogenation)	107·3	110	110
OH (%) (Smith & Bryant)	4·6, 4·67	7·73	5·15
Active H (Zerewitinov)	0·34	0·45	0·303

(iv) The aldehyde (200 g.), ether (200 g.), and di-*n*-butylamine (few drops) were cooled, with stirring, to −20°, and aqueous 10% potassium hydroxide was added dropwise at −15° to −20°. A white *solid* (100 g.) was formed and removed by filtration: it had m. p. *ca.* 80° [Found: H_2O, 12 (Smith and Bryant), 14% (Dean and Stark); CO equiv., 131. $C_7H_{10}O,H_2O$ requires H_2O, 14·1%; CO equiv., 128], and provided the 2 : 4-dinitrophenylhydrazone of 1 : 2 : 3 : 6-tetrahydrobenzaldehyde. The filtrate yielded the aldehyde (78 g.). A cooled mixture of aldehyde and water gave a similar hydrate, m. p. 83—84°.

(c) *Reaction at* 65° *to* ca. 120°. The results are given in Table 4.

In a typical experiment aldehyde (220 g.) and sodium hydroxide (40%; 100 c.c.) were heated under reflux for ½ hr. and the neutral and acid products distilled.

The neutral product gave, on distillation, fractions: (1) (7·7 g.) b. p. 70—80°/2 mm.; (2) (120·8 g.) b. p. 170—175°/2 mm.; residue (2·6 g.). Fraction 1 on redistillation had b. p. 80—85°/18 mm., n_D^{20} 1·4866, and provided a phenylurethane, m. p. 56—57° (from benzene–light petroleum) (Found: C, 73·1; H, 7·3; N, 5·8. Calc. for $C_{14}H_{17}O_2N$: C, 72·7; H, 7·4; N, 6·1%) (m. p. undepressed on admixture with the phenylurethane of 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol obtained by Ponndorf reduction of the aldehyde). The α-naphthylurethane had m. p. 103° (Found: C, 76·5; H, 6·85; N, 5·2. Calc. for $C_{18}H_{19}O_2N$: C, 76·9; H, 6·8; N, 5·0%), and the *p*-nitrobenzoate, m. p. 60—62° (Found: N, 5·4. Calc. for $C_{14}H_{15}O_4N$: N, 5·4%). Fraction 2 was dissolved in benzene and light petroleum was gradually added. A white solid (83·7 g.) crystallised and the filtrate, after evaporation, provided further crystals on storage. The solid glycol (III) had m. p. 98—100° [Found: C, 75·6; H, 10·05;

OH (Smith and Bryant) 13·8%; *M* (Rast), 221; unsaturation equiv. (McIlhiney), 110·5. $C_{14}H_{22}O_2$ requires C, 75·7; H, 9·9; OH, 15·3%; *M*, 222; unsaturation equiv., 111]. It gave no reaction with 2 : 4-dinitrophenylhydrazine hydrochloride, and no carbonyl content (hydroxylamine hydrochloride). The non-crystalline part of this fraction had active hydrogen content (Zerewitinov), 0·84% (calc. for glycol, 0·90%), and infra-red examination indicated no essential difference from the crystalline material.

TABLE 4.

Compound used	Wt. (g.)	Aq. NaOH (c.c.)	Temp.	Reaction time (hr.)	Products (g.): aldehyde and alcohol	trimer	glycol	acid
Aldehyde ...	102	492 (40%)	B. p.	3	3·2	—	61·0	32·8
,, ...	102	492 (40%)	,,	½	3·7	—	57·7	33·7
,, ...	220	100 (40%)	,,	½	7·7	—	120·8	76·0
,, ...	50	250 (4%)	,,	2	32·0	← 5·7 →		5·2
,, ...	50	240 (10%)	,,	3	15·5	← 18·6 →		9·0
,, ...	50	200 (25%)	,,	3	4·1	—	24·9	17·3
,, ...	110	37 g. $Ca(OH)_2$ + 100 g. water	,,	3	48·8	37·4	—	3·4
...	127·5 in MeOH (165 c.c.)	135 g. KOH + 82·5 c.c. water)	70°	2	17·8 *	—	54·4	52·0
,, ...	127·5 in MeOH (165 c.c.)	96·5 g. NaOH + 82·5 c.c. water	70	2	18·5 *	—	52·3	51·5
,, ...	45·5 in MeOH (20 g.)	21·1 g. Na + 125·2 g. MeOH	70	2	5·9 *	—	18·5	16·1
,, ...	46·0 in MeOH (20 g.)	19·8 g. Na + 155 g. MeOH	18	2	5·0 *	—	18·1	10·5
Trimer (II)	50	200 (4%)	B. p.	3	—	45·9	—	2·1
,,	50	200 (10%)	,,	3	—	47·6	—	2·7
,,	117	100 (40%)	,,	1	—	—	76·1	34·2
Solid trimer	30	40 (40%)	,,	3	No reaction			

* Mainly alcohol.

The acid product gave material (76·0 g.), b. p. 125—130°/15 mm., and a residue (2·1 g.). The distillate of 1 : 2 : 3 : 6-tetrahydrobenzoic acid provided a *p-bromophenacyl ester*, m. p. 83—84° (Found: C, 55·3; H, 4·9; Br, 24·6. $C_{15}H_{15}O_3Br$ requires C, 55·7; H, 4·6; Br, 24·8%), and a dibromo-compound, m. p. 82—84° (Found: C, 29·6; H, 3·5; Br, 55·5. Calc. for $C_7H_{10}O_2Br_2$: C, 29·4; H, 3·5; Br, 55·9%).

(d) *Reaction at* 200—240°. These experiments, carried out in a stainless steel rocking autoclave, are reported in Table 5.

TABLE 5.

Reactant	Wt. (g.)	Aq. NaOH (c.c.)	Temp.	Time (hr.)	Neutral products (%): $C_6H_9{\cdot}CH_2{\cdot}OH$	Higher alcohols	Residue	Acid products (%): $C_6H_9{\cdot}CO_2H$	Residue
Aldehyde	90·0	240 (40%)	220°	6	56·3	10·0	24·0	94·7	5·3
,,	45·0	123 (40%)	220	3	54·4	8·05	22·5	90·0	10·0
,,	50·0	Na_2CO_3 (75 g.), water (115 c.c.)	190—230	6	48·2	5·3	21·2	85·0	15·0
,,	59·0	40 (30%)	220—230	6½	65·5	6·2	21·4	86·7	7·6
Liquid glycol	78·5	235·5 (40%)	210—240	6	57·0	17·7	25·3	66·0	20·6
Solid glycol	47·6	143 (40%)	210—230	6	75·4	16·8	5·5	68·4 *	12·8

* 2 : 3 : 4 : 5-Tetrahydro-acid (*p*-bromophenacyl ester).

The fourth of these experiments gave, in addition to the products soluble in water or ether, an insoluble brown solid (7·8 g.) which on recrystallisation from benzene–light petroleum afforded a light brown powder not molten at 285° and giving an ash on ignition. The main products were neutral materials, (1) (19·0 g.) b. p. 82—90°/11 mm., (2) (2·0 g.) b. p. 90—130°/11 mm., (3) (1·8 g.) b. p. >130°/11 mm., and a residue (6·2 g.). Fraction 1 was 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol (phenylurethane). Fraction 3 contained an alcohol (probably the Guerbet product from tetrahydrobenzyl alcohol) [Found: active H (Zerewitinov), 0·47%; unsaturation equiv., 111·9. $C_{14}H_{22}O$ requires active H, 0·48%; unsaturation equiv., 103], which provided a *phenylurethane*, m. p. 140—142° (Found: C, 77·9; H, 8·0; N, 4·4. $C_{21}H_{27}O_2N$ requires C, 77·5; H, 8·3; N, 4·3%). The residue was mainly hydrocarbons (infra-red examination).

Reaction of Alkali with Related Compounds.—The reactions of the trimer and glycol at temperatures up to 240° are given in Tables 4 and 5. The conversion at *ca.* 300° into pimelic acid is mentioned in Table 1. The experiments described below are the reactions, at 300°, of the glycol and alcohol with alkali.

Solid glycol. The glycol (100 g.) and 15·5% aqueous sodium hydroxide (271 c.c.) were heated in the autoclave for 6 hr. at 300°. The neutral product on distillation gave fractions: (1) (6·7 g.) b. p. 30—106°/1 atm., n_D^{20} 1·4745; (2) (0·9 g.) b. p. 70—100°/16 mm., n_D^{20} 1·4713; (3) (8·3 g.) b. p. 100—125°/16 mm., n_D^{20} 1·5139; (4) (3·5 g.), b. p. 140—160°/1 mm.; (5) (5·7 g.) b. p. 160—185°/1 mm.; (6) (3·5 g.) b. p. 185—260°/1 mm.; and a residue (7·5 g.). Fraction 1 showed slight carbonyl and hydroxyl content, and its infra-red spectrum showed it to contain toluene (70%), a *trans*-CH:CH system (5%), some OH, and the remainder mainly 1-methyl*cyclo*hexene. Fraction 2 had an active hydrogen content of 0·78% and carbonyl equiv. 1010, and although hexahydrobenzyl and 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol appeared to be absent infra-red examination suggested the presence of the 2 : 3 : 4 : 5-tetrahydro-alcohol. Fractions 3 and 6 were mainly monosubstituted aromatic hydrocarbons with some unsaturated contaminants. Fractions 4 and 5 crystallised and were largely unchanged glycol. The acid product gave some crystalline pimelic acid (12·7 g.) and the remainder on distillation provided hexahydrobenzoic, 1 : 2 : 3 : 6-tetrahydrobenzoic, pimelic, and higher-boiling acids.

Liquid glycol. The glycol (69·1 g.) and 40% aqueous sodium hydroxide (187 c.c.) were heated at 300° for 6 hr. The neutral products provided mainly hydrocarbons and a fraction (1·8 g.), b. p. 80—100°/16 mm., containing hexahydrobenzyl alcohol (70—75%), 1 : 2 : 3 : 6- (20—25%), and 2 : 3 : 4 : 5-tetrahydrobenzyl alcohol (*ca.* 5%) (infra-red). This fraction afforded the phenylurethane, m. p. and mixed m. p. 74—75°, of hexahydrobenzyl alcohol. The acid products, when distilled, gave a hexahydrobenzoic acid fraction (6·3 g.), which crystallised, and a pimelic acid fraction (12·5 g.).

1 : 2 : 3 : 6-*Tetrahydrobenzyl alcohol.* The alcohol (38·9 g.) and 40% aqueous sodium hydroxide (110 c.c.) were heated at 300° for 6 hr. The neutral products contained no carbonyl compounds and distillation yielded fractions: (1) (5·2 g.) b. p. 100—150°/1 atm.; (2) (2·8 g.) b. p. 90—110°/19 mm.; (3) (2·6 g.) b. p. 110—150°/19 mm.; (4) (3·6 g.) b. p. 150—240°/19 mm.; and a residue (2·4 g.). Fraction 1 contained (infra-red) 35—40% of toluene and some 1-methyl*cyclo*hexene; fraction 2 contained hexahydro- (85%) and 1 : 2 : 3 : 6-tetrahydro-benzyl alcohol (15%), and provided the phenylurethane of the former; fraction 3 contained *ca.* 10% of the 1 : 2 : 3 : 6-tetrahydro-alcohol and hydrocarbons; fraction 4 contained mainly hydrocarbons but also 5—10% of glycol. The acid products contained approx. equal parts of hexahydrobenzoic (with a little tetrahydrobenzoic) and pimelic acid.

Tischtschenko Reaction of the Aldehyde.—Freshly distilled 1 : 2 : 3 : 6-tetrahydrobenzaldehyde was added gradually, with stirring or shaking, to the catalyst (*e.g.*, aluminium *iso*propoxide, 1·5—2·5% calc. on aldehyde) dissolved in a little preformed ester; the temperature of the exothermic reaction was kept below 50°. After the addition was complete stirring was continued until the temperature began to fall without external cooling; then the product was distilled. 1 : 2 : 3 : 6-Tetrahydrobenzyl 1 : 2 : 3 : 6-tetrahydrobenzoate, b. p. 152—153°/7 mm., n_D^{20} 1·4963, was usually formed in 90—95% yield. The aluminium *iso*propoxide could be replaced by aluminium ethoxide or magnesium ethoxide, but larger quantities of these were usually required.

The effect of acid and of temperature on this reaction is shown in Tables 6—8. The aldehyde was estimated by hydroxylamine hydrochloride.

TABLE 6. *Unchanged aldehyde* (%). [Redistilled aldehyde (500 g.) added to the catalyst (aluminium *iso*propoxide, 12·5 g.) in preformed ester (60 g.) during *ca.* 30 min.]

Time (min.) after addn. of aldehyde		0	10	20	40	100
Reaction at :	70°	4·4	—	3·2	1·6	—
	90°	17·4	12·4	8·3	—	5·4
	110°	42·1	—	41·0	39·3	38·7

TABLE 7. *Unchanged aldehyde* (%). [Aldehyde (500 g.), containing 0·5% of tetrahydrobenzoic acid, treated as in Table 6. The addition took 20—40 min.]

Time (min.) after addn. of aldehyde ...		0	10	20	40	70	120
Reaction at :	50°	30·5	10·7	4·9	4·6	2·4	1·0
	60°	22·0	14·0	10·4	8·6	4·5	—
	70°	63·2	38·2	37·0	—	37·0	35·8

TABLE 8.

Aldehyde (50 g.), containing the appropriate amount of added 1 : 2 : 3 : 6-tetrahydrobenzoic acid, added to the catalyst (aluminium *iso*propoxide, 1·25 g.) dissolved in preformed ester (3 g.).

Acid (%, w/w) present in the aldehyde	0	0·78	1·58	3·10	4·77
Unchanged aldehyde (%) after 2 hr. at <40°	0	43·0	57·6	78·6	77·6

In one experiment, the ester (330 g.) was heated with 40% aqueous sodium hydroxide (300 c.c.) for 1 hr. with stirring; the neutral product, on distillation, gave 1 : 2 : 3 : 6-tetrahydrobenzyl alcohol (137 g.) and a residue (3·5 g.), whilst the acid product consisted of 1 : 2 : 3 : 6-tetrahydrobenzoic acid (183·3 g.) and a residue (6·0 g.).

The authors thank Mr. Philpotts for infra-red spectroscopic examination of some of their products, the Pilot Plant Division (Tonbridge) for production of the aldehyde, and the Directors of the Company for permission to publish this paper.

THE DISTILLERS COMPANY LIMITED, RESEARCH AND DEVELOPMENT DEPARTMENT,
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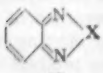
A New Route to N-Substituted o-Phenylenediamines.

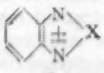
By E. S. LANE and C. WILLIAMS.

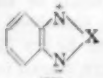
[Reprint Order No. 6048.]

Phenyl-lithium reacts with benzo-2 : 1 : 3-thiadiazole or its selenium analogue to give diphenyl sulphide (or selenide) and *N*-phenyl-*o*-phenylenediamine. With the oxygen analogue, further substitution can occur and 2-anilinotriphenylamine has been obtained. A tentative reaction scheme is proposed to account for the formation of these compounds.

DIRECT *N*-substitution of *o*-diamines has received little attention. *N*-Methylation of *o*-phenylenediamine by methyl iodide has been carried out by Brown and Nelson (*J. Amer. Chem. Soc.*, **1953**, **75**, 24) but the method has not been extended to higher homologues and is inapplicable to aryl substituents. The method presented below provides a new route to *N*-substituted *o*-diamines and involves the reaction of phenyl-lithium with benzo-2 : 1 : 3-thiadiazole (I; X = S) or its selenium and oxygen analogues. With the first it gives


(I)


(Ia)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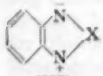
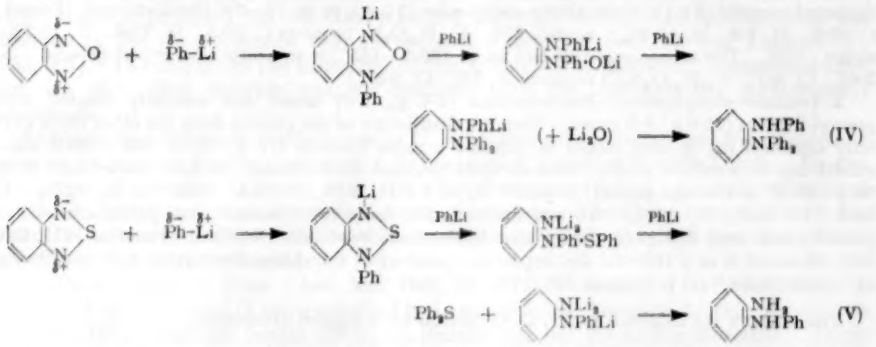

(III)

diphenyl sulphide and *N*-phenyl-*o*-phenylenediamine (V), and with benzo-2 : 1 : 3-selenadiazole (I; X = Se) it gives diphenyl selenide and the diamine (V). With 4 : 7-diethoxybenzo-2 : 1 : 3-selenadiazole it gives diphenyl selenide and 2-amino-3-anilinoquinol diethyl ether. Use of a larger proportion of phenyl-lithium did not cause further substitution of the *o*-diamine. Benzofurazan (I; X = O) and an excess of phenyl-lithium gave a small quantity of diphenyl and 55% of 2-anilinotriphenylamine (IV), the only convenient route to this compound.

The normal mode of addition of an organometallic compound to an organic system places the organic residue on the most positive atom. Pauling ("Nature of the Chemical Bond," Cornell Univ. Press, New York, 1949, p. 60) gives as the order of decreasing electronegativities: O 3·5, N 3·0, S 2·5, Se 2·4, so reactions with phenyl-lithium should be: $>N{\cdot}O^- \longrightarrow >NPh + LiO^-$; $>N{\cdot}S^- \longrightarrow >NLi + RS^-$; $>N{\cdot}Se^- \longrightarrow >NLi + RSe^-$. If it is assumed that the structures (II) and (III) provide a major portion of the canonical forms contributing to the hybrid (I*a*),* then the annexed reactions account for the products

* This is not an improbable assumption. The compounds involved are partially mesoionic (Baker, Ollis, and Poole, *J.*, 1950, 1546) and the hybrid will contain a large ionic contribution, particularly in the polarised state of the transition complex.

isolated. Selenium would be expected to behave similarly to sulphur as their electronegativities are nearly equal. A higher yield is obtained from the sulphur compound than from the selenium compound but this may be offset by the relatively easier accessibility of



the latter which is conveniently prepared in very good yields by reaction of *o*-diamines with selenious acid (Hinsberg, *Ber.*, 1889, **22**, 863, 2897; 1890, **23**, 1397; Heinemann, D.-R.P. 261,412; Lane and Williams, *J.*, 1954, 2978).

Experimental

The equivalent weights of the amines described below were determined by titration in glacial acetic acid with 0·1N-perchloric acid, with crystal-violet as indicator. The equivalent weight of the *N*-phenyl-*o*-phenylenediamine hydrochloride was determined by titration in dimethylformamide with sodium methoxide in benzene–methanol with thymol-blue as indicator.

Action of Phenyl-lithium on Benzo-2 : 1 : 3-thiadiazole.—Benzo-2 : 1 : 3-thiadiazole (27·2 g., 0·2 mole) in ether (100 ml.) was added dropwise to a stirred solution of phenyl-lithium (59 g., 0·7 mole) in ether (100 ml.) under nitrogen. After 2 hr., water (100 ml.) was added to the deep green solution. The red ether layer was run off and evaporated; the residual red tar was distilled and collected in the following fractions: (i) (36 g.) b. p. 132—136°/1 mm., n_D^{21} 1·6314; (ii) b. p. 136—160°/1 mm., a mixture of (i) and (iii); (iii) (27 g.) b. p. 162—166°/1 mm., m. p. 78°. Fraction (i) was diphenyl sulphide (b. p. 148·5—149·5°/12 mm., $n_D^{18\cdot5}$ 1·635); oxidation with hydrogen peroxide in acetic acid gave diphenyl sulphone, m. p. and mixed m. p. 128°. Fraction (ii) was purified by shaking its ethereal solution with 10% hydrochloric acid; a crystalline precipitate of *N-phenyl-o-phenylenediamine hydrochloride*, m. p. 115·5—117° (decomp.), was filtered off (Found: N, 12·7; Cl, 16·35%; equiv., 222. $C_{12}H_{13}N_2Cl$ requires N, 12·7; Cl, 16·1%; equiv., 220); a small quantity of diphenyl sulphide, b. p. 294—295°/760 mm., was obtained on distillation of the filtrate. Fraction (iii) was purified by crystallisation from ethanol; *N*-phenyl-*o*-phenylenediamine had m. p. 79—80° (Found: C, 78·3; H, 6·4; N, 15·3%; equiv., 183. Calc. for $C_{12}H_{12}N_2$: C, 78·3; H, 6·5; N, 15·2%; equiv., 184); heating it with lead oxide gave phenazine, m. p. and mixed m. p. 171—172° (Found: N, 15·3. Calc. for $C_{12}H_8N_2$: N, 15·55%).

Action of Phenyl-lithium on Benzo-2 : 1 : 3-selenadiazole.—Benzo-2 : 1 : 3-selenadiazole (18·3 g., 0·1 mole) in ether (120 ml.) was similarly treated with phenyl-lithium (29·4 g., 0·35 mole) and worked up, giving fractions: (i) b. p. 88—110°/0·5 mm.; (ii) (21 g.) b. p. 112—136°/0·5 mm.; and (iii) (10 g.) b. p. 138—140°/0·5 mm. Fraction (i) was a small amount of unchanged material; fraction (ii) was redistilled and gave as a main fraction, b. p. 120°/2·5 mm., diphenyl selenide (Found: C, 62·0; H, 3·9. Calc. for $C_{12}H_{10}Se$: C, 61·8; H, 4·3%), characterised by conversion into the dibromide, m. p. 151° (decomp.) (Found: C, 37·3; H, 2·6; Br, 41·3. Calc. for $C_{12}H_{10}Br_2Se$: C, 36·7; H, 2·55; Br, 40·6%) [Edwards, Gaythwaite, Kenyon, and Phillips (*J.*, 1928, 2302) gave m. p. 154° (decomp.)]. Fraction (iii), crystallised from ethanol, had m. p. 79—80° (equiv., 183), not depressed on admixture with authentic *N*-phenyl-*o*-phenylenediamine.

4 : 7-*Diethoxybenzo-2 : 1 : 3-selenadiazole.*—Equimolar amounts of 2 : 3-diaminoquinol diethyl ether hydrochloride (Lane and Williams, *J.*, 1953, 4187) and selenious acid were heated together in water (steam-bath) for 1 hr., giving a quantitative yield of this *base*, m. p. 152—152·5° (yellow

platelets from benzene) (Found: C, 44·3; H, 4·1; N, 10·3. $C_{16}H_{12}O_2N_2Se$ requires C, 44·3; H, 4·4; N, 10·3%).

2-Amino-3-anilinoquinol Diethyl Ether.—The foregoing compound (6·4 g., 0·024 mole) was treated as described above with phenyl-lithium (8·4 g., 0·1 mole). Working up as before gave diphenyl selenide (5 g.) and the above *amino-ether* (2·5 g.), m. p. 77—79° (from ethanol) (Found: C, 70·6; H, 7·3; N, 10·3%; equiv., 275. $C_{16}H_{20}O_2N_2$ requires C, 70·5; H, 7·35; N, 10·3%; equiv., 272). The *monoperchlorate* had m. p. 153·5—155° (from acetic acid–ether) (Found: N, 7·65; Cl, 9·7. $C_{16}H_{21}O_6N_2Cl$ requires N, 7·5; Cl, 9·5%).

2-Anilinotriphenylamine.—Benzofurazan (8·4 g., 0·07 mole) was similarly treated with phenyl-lithium (42·0 g., 0·5 mole). Vacuum-distillation of the residue from the ether layer gave only diphenyl (m. p. and mixed m. p.) and a main fraction (13 g.), b. p. 226—230/2 mm., solidifying to a yellow solid. After 4 crystallisations from ethanol the base named had m. p. 94·5—95·5° (colourless plates) (Found: C, 85·1; H, 5·85; N, 8·4. Calc. for $C_{24}H_{20}N_2$: C, 85·6; H, 5·95; N, 8·3%). It was insufficiently basic for titration with perchloric acid in glacial acetic acid and gave a deep blue Liebermann reaction. Wieland (*Annalen*, 1911, **381**, 206) obtained it as a thermal decomposition product of tetraphenylhydrazine and described it as "amorphous," m. p. "about 85°."

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Interaction of Boron Trichloride with Chloro-alcohols and with Cyclic Ethers.

By J. D. EDWARDS, W. GERRARD, and M. F. LAPPERT.

[Reprint Order No. 6065.]

Studies on boron trichloride–alcohol systems have been extended to include examples in which the alkyl group contains chlorine. By interaction in appropriate proportion of the respective alcohols with boron trichloride, tri-2-chloroethyl and tri-4-chlorobutyl borate, di-2-chloroethyl chloroboronate, and 2-chloroethyl and 4-chlorobutyl dichloroboronites were prepared. The alkoxyboron chlorides disproportionate reversibly and form adducts with pyridine. 4-Chlorobutyl dichloroboronite unlike the 2-chloroethoxyboron chlorides, but like other alkoxyboron chlorides, decomposes to form the chloroalkane, boron trichloride, and boron trioxide. Ethylene oxide and boron trichloride gave no 1 : 1 adduct even at −80°, but afforded 2-chloroethyl dichloroboronite. From the tetrahydrofuran–boron trichloride complex, 4-chlorobutyl dichloroboronite (or its decomposition products) was obtained only on heating. Reactions are described which differentiate dichloroboronites from their isomeric 1 : 1 complexes.

TRI-2-CHLOROETHYL borate and tri-4-chlorobutyl borate have been obtained quantitatively by the interaction of boron trichloride (1 mol.) with 2-chloroethanol (3 mols.) and 4-chlorobutan-1-ol (3 mols.) respectively. In the 2-chloroethyl series, the intermediate alkoxyboron chlorides, $RO{\cdot}BCl_2$ and $(RO)_2BCl$, were prepared by the appropriate reaction (1)—(4):

$$Cl{\cdot}[CH_2]_2{\cdot}OH + BCl_3 \longrightarrow Cl{\cdot}[CH_2]_2{\cdot}O{\cdot}BCl_2 + HCl \quad (1)$$

$$2Cl{\cdot}[CH_2]_2{\cdot}OH + BCl_3 \longrightarrow (Cl{\cdot}[CH_2]_2{\cdot}O)_2BCl + 2HCl \quad (2)$$

$$(Cl{\cdot}[CH_2]_2{\cdot}O)_3B + 2BCl_3 \rightleftharpoons 3Cl{\cdot}[CH_2]_2{\cdot}O{\cdot}BCl_2 \quad (3)$$

$$2(Cl{\cdot}[CH_2]_2{\cdot}O)_3B + BCl_3 \rightleftharpoons 3(Cl{\cdot}[CH_2]_2{\cdot}O)_2BCl \quad (4)$$

Both 2-chloroethyl dichloroboronite and di-2-chloroethyl chloroboronate disproportionate on being heated under reflux at reduced pressure:

$$2Cl{\cdot}[CH_2]_2{\cdot}O{\cdot}BCl_2 \rightleftharpoons BCl_3 + (Cl{\cdot}[CH_2]_2{\cdot}O)_2BCl \quad (5)$$

$$2(Cl{\cdot}[CH_2]_2{\cdot}O)_2BCl \rightleftharpoons (Cl{\cdot}[CH_2]_2{\cdot}O)_3B + Cl{\cdot}[CH_2]_2{\cdot}O{\cdot}BCl_2 \quad (6)$$

and in consequence distillation of these compounds was invariably accompanied by disproportionation.

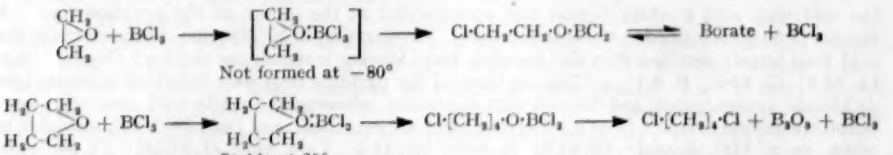
These results differ from those obtained with other alkoxyboron chlorides (Wiberg and Sütterlin, *Z. anorg. Chem.*, **1931**, **202**, 1, 22, 31; Gerrard and Lappert, *J.*, **1951**, 2545), where disproportionation has not been reported, although similar disproportionation was observed in the phenoxyboron chloride systems (Colclough, Gerrard, and Lappert, *J.*, 1955, 907). In contrast to the behaviour of the butoxyboron chlorides (Gerrard and Lappert, *loc. cit.*), alkyl chloride was not obtained from the corresponding 2-chloroethyl compounds.

2-Chloroethyl dichloroboronite formed a 1 : 1 complex with pyridine, and there was some evidence to support the formation of a 1 : 2 complex, $Cl{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}BCl_2,2py$. By the interaction of pyridine (1 mol.) with the chloroboronate (1 mol.) a small amount of borate was isolated, the main product being a mixture of addition compounds of the chloroboronate and dichloroboronite with pyridine, in which the 1 : 1 pyridine–chloroboronate complex preponderated.

Martin and Mako (*J. Amer. Chem. Soc.*, 1951, **73**, 2674) by reaction of boron trichloride (1 mol.) and 2-chloroethanol (1 mol.) obtained hydrogen chloride, boron trichloride, the chloroboronate (15%), and the borate (38%) on distillation, but no dichloroboronite. These results are now understandable in view of the ready disproportionation of the dichloroboronite. Tri-2-chloroethyl borate has previously been prepared (90%) by Jones, Thomas, Pritchard, and Bowden (*J.*, **1946**, 825) from boron trioxide and 2-chloroethanol.

4-Chlorobutyl dichloroboronite was prepared by reactions analogous to (1) and (3), but in contrast to the 2-chloroethyl compound it decomposed when heated to 1 : 4-dichlorobutane, boron trichloride, and boron trioxide: $3Cl{\cdot}[CH_2]_4{\cdot}O{\cdot}BCl_2 \longrightarrow 3Cl{\cdot}[CH_2]_4{\cdot}Cl + BCl_3 + B_2O_3$. There was also some disproportionation during distillation. A 1 : 1 pyridine–dichloroboronite complex was formed.

The dichloroboronites (2-chloroethyl and 4-chlorobutyl) were also obtained by the reaction of boron trichloride with ethylene oxide or tetrahydrofuran (for reaction of boron trichloride with dialkyl ethers, see Ramser and Wiberg, *Ber.*, **1930**, **63**, 1136, and Gerrard and Lappert, *J.*, 1952, 1486) but a difference was noted between the two systems. Ethylene oxide (1 mol.) and boron trichloride (1 mol.) at −80° afforded the ester, as was evident from the identity of its properties with early specimens. Successive addition of ethylene oxide (1 mol.) and 2-chloroethanol (2 mols.) to boron trichloride (1 mol.) at −80° gave only tri-2-chloroethyl borate and hydrogen chloride, indicating that even at this temperature no 1 : 1 ethylene oxide–boron trichloride complex was formed. Tetrahydrofuran on the other hand gave a solid 1 : 1 complex stable at 20°, which only on heating gave the isomeric dichloroboronite or its decomposition products depending on the conditions of experiment. The



evidence for the existence of the 1 : 1 tetrahydrofuran complex was its hydrolysis and alcoholysis (*n*-butanol) to yield tetrahydrofuran, hydrogen chloride, and boric acid (or tri-*n*-butyl borate). Moreover all the chlorine was available as hydrogen chloride after hydrolysis with cold water, indicating the presence of three boron–chlorine bonds.

These conclusions differ from those of Grimley and Holliday (*J.*, **1954**, 1212) who considered that both ethers formed 1 : 1-complexes, which differed only in that the ethylene oxide complex was said to dissociate reversibly $[(CH_2)_2O,BCl_3 \rightleftharpoons (CH_2)_2O + BCl_3$; shown by a saturated vapour-pressure–temperature curve], whereas the tetrahydrofuran complex dissociated irreversibly. We are of the opinion that their vapour-pressure measurements in the ethylene oxide system represented the reversible disproportionation of

2-chloroethyl dichloroboronite. In addition, since aqueous hydrolysis of the latter gives two-thirds and alkaline hydrolysis all of its chlorine as chloride ion, their use of sodium hydroxide for chlorine estimation would not have distinguished between a 1 : 1 complex and the isomeric dichloroboronite. In the tetrahydrofuran system hydrogen chloride was stated to be one of the products, but we could not confirm this.

Experimental

Chlorine attached to boron was hydrolysed (except in the case of monopyridine–boron trichloride) by cold water (e.h. Cl hereafter). Chlorine attached to carbon was hydrolysed in boiling aqueous or alcoholic alkaline solution (total chlorine is designated Cl hereafter).

Interaction of Boron Trichloride (1 Mol.) and 2-Chloroethanol (1, 2, and 3 Mols., severally).—(*a*) The alcohol (80·1 g., 3 mols.) was added slowly to the trichloride (47·1 g., 1 mol.) at −80° and the whole kept overnight at −80°. Hydrogen chloride was then removed at the pump. The residue (98·7 g.) gave on distillation tri-2-chloroethyl borate [93·6 g., 93·6% based on : $3ROH + BCl_3 \longrightarrow (RO)_3B + 3HCl$], b. p. 70°/0·1 mm. (Found : B, 4·39. Calc. for $C_6H_{12}O_3Cl_3B$: B, 4·33%).

(*b*) The alcohol (4·05 g., 1 mol.) was added to the trichloride (5·85 g., 1 mol.) at −80°. After 20 min. at −80°, the mixture was allowed to warm to 20°, whereupon hydrogen chloride (1·69 g., 93% based on : $ROH + BCl_3 \longrightarrow RO{\cdot}BCl_2 + HCl$) was evolved. At 20°/0·5 mm., *2-chloroethyl dichloroboronite* (5·20 g.), n_D^{20} 1·4429, d^{18} 1·358 (Found : e.h. Cl, 43·9; Cl, 66·2; B, 6·7. $C_2H_4OCl_2B$ requires e.h. Cl, 44·0; Cl, 66·0; B, 6·7%), distilled, leaving a residue (1·95 g.), n_D^{20} 1·4560 (Found : e.h. Cl, 15·6; Cl, 51·0; B, 5·3%). Some material was lost during distillation (probably boron trichloride by disproportionation of the dichloroboronite).

(*c*) The alcohol (6·80 g., 2 mols.) was added slowly to the trichloride (4·90 g., 1 mol.) at −80°. Volatile material was removed (15°/15 mm.), leaving di-2-chloroethyl chloroboronate [8·45 g., 98·7% based on : $2ROH + BCl_3 \longrightarrow (RO)_2BCl + 2HCl$] (Found : e.h. Cl, 16·9; B, 5·4. Calc. for $C_4H_8O_2Cl_3B$: e.h. Cl, 17·3; B, 5·3%). Distillation of this material led to disproportionation.

Interaction of Boron Trichloride and Tri-2-chloroethyl Borate.—(*a*) The trichloride (4·05 g., 2 mols.) at −39° was added to the borate (4·30 g., 1 mol.) at −5°. At 20°/0·5—1 mm., 2-chloroethyl dichloroboronite (6·10 g.), n_D^{20} 1·4433, d_4^{17} 1·361 (Found : e.h. Cl, 44·8; B, 6·8%), distilled from the product and condensed at −80°, leaving a residue (1·55 g.) (Found : e.h. Cl, 20·0; B, 5·6%). The loss in weight (0·70 g.) is attributed to boron trichloride.

(*b*) The borate (6·38 g., 2 mols.), dissolved in *n*-pentane (10 ml.), was added to boron trichloride (1·50 g., 1 mol.) at −80°. The pentane was removed (20°/10 mm.), leaving a residue (7·75 g.) of di-2-chloroethyl chloroboronate, n_D^{20} 1·4551, d_4^{18} 1·320 (Found : e.h. Cl, 16·8; Cl, 51·6; B, 5·3. Calc. for $C_4H_8O_2Cl_3B$: e.h. Cl, 17·3; Cl, 51·9; B, 5·3%).

Reactions of 2-Chloroethyl Dichloroboronite.—(a) *Disproportionation.* The dichloroboronite (4·10 g.) was heated under reflux at 70°/14 mm. In series with the condenser were, first, a trap at −80° and then a trap containing pyridine. After 2·33 hr. a condensate had collected in the cold trap, and a white deposit had accumulated at the mouth of the pyridine trap. A residue (2·50 g.) remained in the reaction flask. On warming to 20°/760 mm. the contents of the cold trap largely distilled into the pyridine trap, leaving a remainder (0·25 g.) (Found : e.h. Cl, 34·9; Cl, 62·0; B, 6·7%). The contents of the pyridine trap were dissolved in methylene dichloride, concentrated, and treated with *n*-pentane, whereupon a white solid, monopyridine–boron trichloride complex (1·84 g.) (Gerrard and Lappert, *Chem. and Ind.*, 1952, **53**), insoluble in water, m. p. 115° (Found : Cl, 54·3; B, 5·49; py, 41·1. Calc. for $C_5H_5NCl_3B$: Cl, 54·2; B, 5·50; py, 40·2%), was deposited. The residue from the reaction flask afforded on distillation : (1) (0·80 g.), b. p. up to 70°/0·2—0·1 mm., n_D^{20} 1·4500 (Found : e.h. Cl, 11·0; Cl, 49·7; B, 4·9%); (2) tri-2-chloroethyl borate (0·60 g.), b. p. 70°/0·1 mm., n_D^{20} 1·4550 (Found : Cl, 43·2; B, 4·35%); and the dichloroboronite (0·80 g.), n_D^{20} 1·4468 (Found : e.h. Cl, 39·0; Cl, 63·9; B, 6·4%), condensed at −80°.

(b) *Reaction with pyridine* (1 : 1). Pyridine (2·50 g., 1 mol.), in methylene dichloride (30 ml.), was added to the dichloroboronite (5·15 g., 1 mol.) at −80°. The solvent was removed (20°/15 mm.) and the oily product thrice washed with *n*-pentane, solvent traces being removed under reduced pressure. The residue (7·65 g., 100%) was the *monopyridine–2-chloroethyl dichloroboronite complex* (Found : e.h. Cl, 29·2; Cl, 42·7; B, 4·3; C_5H_5N, 32·4. $C_7H_9ONCl_2B$ requires e.h. Cl, 29·5; Cl, 44·3; B, 4·5; C_5H_5N, 32·9%).

(c) *Reaction with pyridine* (1 : 2). To the dichloroboronite (4·00 g., 1 mol.) in pentane (20

ml.) pyridine (4·20 g., 2 mols.) was added. A sticky solid precipitate formed which after filtration and repeated washing with *n*-pentane weighed 7·57 g. This appeared to be a dipyridine–2-chloroethyl dichloroboronite complex (Found: e.h. Cl, 21·1; C_5H_5N, 45·6. Calc. for $C_{12}H_{14}ON_2Cl_3B$: e.h. Cl, 22·2; C_5H_5N, 49·5%). It was hydrolysed in water.

Reactions of Di-2-chloroethyl Chloroboronate.—(a) *Disproportionation.* The chloroboronate (5·10 g.) was heated (7·8 hr.) under reflux at 100—120°/1·0 mm. The reflux condenser was connected to a trap at −80° in which a condensate of crude dichloroboronite (1·10 g.), n_D^{20} 1·4450 (Found: e.h. Cl, 40·0; Cl, 63·0; B, 6·7%), recondensed at 20°/1 mm. (n_D^{20} 1·4430) (Found: e.h. Cl, 44·1; Cl, 65·5; B, 6·5%), had collected. The residue (3·60 g.) in the reaction vessel was the impure borate, n_D^{20} 1·4545 (Found: e.h. Cl, 2·25; Cl, 43·6; B, 4·4%). A portion (3·25 g.) afforded on distillation: (1) a forerun (0·5 g.), b. p. 52—71°/0·1 mm., n_D^{20} 1·4556 (Found: e.h. Cl, 4·65; Cl, 45·5; B, 4·7%); (2) pure tri-2-chloroethyl borate (2·55 g.), b. p. 71°/0·1 mm., n_D^{20} 1·4547 (Found: Cl, 42·8; B, 4·35%); and a residue (0·15 g.).

(b) *Reaction with pyridine.* The chloroboronate (2·00 g., 1 mol.) in *n*-pentane (10 ml.) was added to pyridine (0·77 g., 1 mol.) in pentane (10 ml.) cooled to −10°. A white solid was precipitated which at 20° became a faintly yellow oil. The solvent was decanted off and the oil washed with *n*-pentane (10 ml.). Traces of solvent were removed (20°/10 mm.), leaving a residue (2·34 g.) which was probably substantially a monopyridine–di-2-chloroethyl chloroboronate complex (Found: e.h. Cl, 13·7; Cl, 35·9; C_5H_5N, 29·7. Calc. for $C_9H_{12}O_2NCl_3B$: e.h. Cl, 12·5; Cl, 37·5; C_5H_5N, 27·8%). Concentration of the pentane washings left a residue (0·32 g.) of tri-2-chloroethyl borate (Found: e.h. Cl, none; Cl, 41·6; B, 4·5%).

Interaction of Ethylene Oxide (1 Mol.) with Boron Trichloride (1 Mol.).—(a) Ethylene oxide (2·75 g., 1 mol.), cooled to −40°, was added slowly with continuous shaking to the trichloride (7·50 g., 1 mol.) at −75°. The crude product (10·1 g.) was 2-chloroethyl dichloroboronite, n_D^{20} 1·4455, d_4^{23} 1·380 (Found: e.h. Cl, 46·0; Cl, 68·2; B, 6·8%). Distillation (20°/2 mm.) gave a purer specimen of the dichloroboronite, n_D^{20} 1·4443, d_4^{19} 1·365 (Found: e.h. Cl, 45·0; Cl, 66·6; B, 6·7%), and a residue, largely di-2-chloroethyl chloroboronate, indicating disproportionation as already shown.

(b) Ethylene oxide (1·88 g., 1 mol.) in methylene dichloride (25 ml.), cooled to −39°, was added to boron trichloride (5·00 g., 1 mol.) in methylene dichloride (10 ml.) at −80°. 2-Chloroethanol (6·86 g., 2 mols.) was added to this cooled mixture. On removal of solvent (at 20°/15 mm.), a residue of tri-2-chloroethyl borate (10·6 g., 100%) (Found: Cl, 42·5; B, 4·2%) remained which was distilled, affording the pure borate (9·95 g., 93%), b. p. 96—97·5°/0·8 mm., n_D^{20} 1·4555 (Found: Cl, 42·8; B, 4·3%). The yield is based on: $RO{\cdot}BCl_2 + 2ROH \longrightarrow (RO)_3B + 2HCl$.

Interaction of 4-Chlorobutanol with Boron Trichloride.—(a) The alcohol (9·9 g., 3 mols.) in *n*-pentane (5 ml.) was added to the trichloride (3·55 g., 1 mol.) at −80°. At 20°/10 mm., hydrogen chloride and *n*-pentane were removed, leaving a residue [10·25 g., 100% based on: $3ROH + BCl_3 \longrightarrow (RO)_3B + 3HCl$] which on distillation afforded: (1) a forerun (0·8 g.), b. p. up to 136°/0·1 mm., n_D^{20} 1·4590 (Found: Cl, 30·3; B, 2·9%); (2) *tri-4-chlorobutyl borate* (9·0 g.), b. p. 136—140°/0·1 mm., n_D^{21} 1·4618, d_4^{20} 1·350 (Found: Cl, 32·0; B, 3·2. $C_{12}H_{24}O_3Cl_3B$ requires Cl, 32·0; B, 3·2%); and a residue (0·20 g.).

(b) The alcohol (2·90 g., 1 mol.) was added to the trichloride (3·15 g., 1 mol.) at −80°. Hydrogen chloride was evolved on warming and was trapped in potassium hydroxide (chloride ion, 0·367 g., 97·4% based on: $BCl_3 + ROH \longrightarrow RO{\cdot}BCl_2 + HCl$). The residue (5·00 g., 98·6%) was *4-chlorobutyl dichloroboronite*, n_D^{20} 1·4522, d_4^{20} 1·254 (Found: e.h. Cl, 36·5; Cl, 55·9; B, 5·65. $C_4H_8OCl_3B$ requires e.h. Cl, 37·5; Cl, 56·3; B, 5·7%). Distillation of a portion (4·3 g.) under reduced pressure apparently led to disproportionation, giving: (1) (0·88 g.), b. p. up to 68°/1·0 mm., n_D^{20} 1·4541 (Found: e.h. Cl, 30·1; Cl, 52·5; B, 5·1%); (2) (0·35 g.), b. p. 68—74°/1·0 mm., n_D^{20} 1·4615 (Found: e.h. Cl, 23·0; B, 5·2%); and a residue (1·70 g.), n_D^{20} 1·4630 (Found: e.h. Cl, 7·72; Cl, 36·4; B, 3·9%). A condensate (0·35 g.), collected in a trap at −80°, had n_D^{20} 1·4499 (Found: e.h. Cl, 13·37; Cl, 53·9; B, 2·0%). Some material (1·10 g.), probably boron trichloride, was lost during distillation.

Interaction of Boron Trichloride (2 Mols.) with 4-Chlorobutyl Borate (1 Mol.).—The borate (4·4 g., 1 mol.) in methylene dichloride (10 ml.) was added to the trichloride (3·1 g., 2 mols.) at −80°. After 1 hr. at −80° the mixture was allowed to warm to 20° and volatile matter was removed (20 min. at 17 mm.). The residue (7·31 g., 97·4%) was 4-chloroethyl dichloroboronite (Found: e.h. Cl, 34·4; Cl, 54·9; B, 5·55%).

Reactions of 4-Chlorobutyl Dichloroboronite.—(a) *Pyrolysis.* The dichloroboronite (5·40 g.) was heated for 5 hr. in a sealed tube at 100°. The tube was cooled to −80° and opened, and the clear liquid contents were allowed to warm, the outlet being attached to water absorption-bottles.

No appreciable evolution of gas was observed, but, on heating, boron trichloride (80%) was evolved and a white precipitate formed simultaneously. Distillation of the residue afforded a liquid (3·5 g.) and a white solid (0·8 g.) which was largely boron trioxide (0·7 g. of boron trioxide required for the reaction: $3RO{\cdot}BCl_3 \longrightarrow B_2O_3 + BCl_3 + 3RCl$). The distillate was dissolved in ether, washed free from traces of boron trichloride, dried ($CaCl_2$), and distilled, giving 1 : 4-dichlorobutane (2·9 g., 80%), b. p. 150—152°/760 mm., n_D^{20} 1·4537 (Found: Cl, 54·3. Calc. for $C_4H_8Cl_2$: Cl, 55·7%).

In separate experiments the rate of decomposition was estimated by heating individual samples in sealed tubes at 100°. These were broken under water in a stoppered flask and the equivalence ratio of e.h. Cl to boron was determined, being initially 2 : 1 and finally 1 : 1.

e.h. Cl : B	1·94	1·91	1·76	1·59	1·44	1·37	1·28	1·15	1·13	1·05	1·01
Time (min.) ...	10	20	30	40	50	60	70	80	90	110	145

(b) *Reaction with pyridine.* The borate (1·70 g., 1 mol.) in *n*-pentane (10 ml.) was added to the trichloride (1·20 g., 2 mols.) at −80°. After 20 min. at 20°, the solution, cooled to −15°, was treated with pyridine (1·21 g., 3 mols.) in *n*-pentane (10 ml.). A pale yellow oil and some white solid were precipitated. The pentane was removed (20°/10 mm.) and the residue (4·10 g.) was washed twice with pentane. Washing with water left the insoluble monopyridine–boron trichloride complex (0·22 g.), m. p. 115°. The water-soluble portion (3·75 g.) was substantially a *monopyridine–4-chlorobutyl dichloroboronite complex* (Found: e.h. Cl, 24·5; Cl, 37·7; B, 4·1; C_5H_5N, 29·0. $C_9H_{13}ONCl_3B$ requires e.h. Cl, 26·4; Cl, 39·7; B, 4·0; C_5H_5N, 29·4%).

Interaction of Tetrahydrofuran (1 Mol.) with Boron Trichloride (1 Mol.).—Tetrahydrofuran (3·35 g., 1 mol.) in *n*-pentane (10 ml.) was added to the trichloride (5·45 g., 1 mol.) in pentane (20 ml.) at −80°. The reaction afforded the white solid, monotetrahydrofuran–boron trichloride complex (8·3 g., 94%), m. p. 88—95° (decomp.) (Found: e.h. Cl, 55·3; B, 5·85. Calc. for $C_4H_8OCl_3B$: e.h. Cl, 56·3; B, 5·7%).

Reactions of the Monotetrahydrofuran–Boron Trichloride Complex.—(a) *With* n-*butanol.* The complex (13·25 g., 1 mol.) was treated with *n*-butanol (15·55 g., 3 mol.) at 20°. Hydrogen chloride was vigorously evolved. After 20 hr. at 20°, material (3·30 g.) volatile at 20°/15 mm. was collected in a trap at −80°. This, after treatment first with lead carbonate and subsequently with anhydrous magnesium sulphate, yielded on distillation tetrahydrofuran (3·10 g., 62%), b. p. 64·5—66°/760 mm., n_D^{20} 1·4063, d_4^{20} 0·885. The remainder yielded tri-*n*-butyl borate (13·00 g., 79%), b. p. 113°/13 mm., n_D^{20} 1·4090 (Found: B, 4·70. Calc. for $C_{12}H_{27}O_3B$: B, 4·72%), on distillation [yields are based on: $C_4H_8O,BCl_3 + 3Bu^nOH \longrightarrow (Bu^nO)_3B + 3HCl + C_4H_8O$].

(b) *Hydrolysis.* The complex (8·00 g.) was treated with water (25 ml., large excess). Tetrahydrofuran (1·55 g., 51·0%), b. p. 64°/760 mm., n_D^{20} 1·4058, d_4^{21} 0·902, was distilled from the reaction mixture.

(c) *Pyrolysis.* The complex (6.00 g.) was heated (0·33 hr. at 100°, and a further 3·25 hr. at 120—135°) at atmospheric pressure. Volatile material was collected in a trap (−80°) connected in series with a potassium hydroxide absorption tube. Boron trichloride (1·02 g., 82·3%) collected in the cooled trap (Found: e.h. Cl, 90·8; B, 9·2. Calc. for Cl_3B: e.h. Cl, 90·8; B, 9·2%). There was a negligible amount of chloride in the potassium hydroxide absorption tube. The residue from the pyrolysis was extracted with hot *n*-pentane (2 × 25 ml.), leaving a dark solid (1·13 g.) (Found: e.h. Cl, 11·0; B, 22·0, equiv. to 70% of the total boron in the system) which may have contained much boron trioxide. From the pentane extract, 1 : 4-dichlorobutane (3·15 g., 78%), b. p. 150°/760 mm., n_D^{20} 1·4532, d_4^{20} 1·132 (Found: Cl, 53·5%), and a small residue (0·22 g.) were obtained [yields are based on: $3C_4H_8O,BCl_3 \longrightarrow 3Cl(CH_2)_4Cl + BCl_3 + B_2O_3$].

In a further experiment a sample of the complex was heated (4·3 hr.) in a sealed tube at 100°. The tube was broken under water in a stoppered flask and the e.h. chlorine and boron estimated. The e.h. chlorine had dropped to one-third of that in the starting material and the equivalence ratio of e.h. chlorine to boron was exactly 1 : 1, as required by the above equation.

(d) *Pyrolysis at reduced pressure.* The complex (6·45 g.) was heated for 2 hr. at 100—120°/1—2 mm., during which a condensate (3·20 g.), n_D^{20} 1·4520 (Found: e.h. Cl, 26·8; B, 4·02%; equivalence ratio of e.h. Cl : B, 2 : 1), believed to be a mixture of 1 : 4-dichlorobutane and 4-chlorobutyl dichloroboronite, had collected at −80°. To a sample (2·80 g.) in methylene dichloride (20 ml.), 4-chlorobutanol (2·30 g., 2 mol. per mol. of boron in condensate) was added at −80°. The solvent and hydrogen chloride were removed (15°/17 mm.) and the residue distilled, affording tri-4-chlorobutyl borate (2·75 g., 79% based on conversion of boron in condensate

into borate), b. p. 140°/0·3 mm., n_D^{20} 1·4620, d_4^{20} 1·370 (Found : Cl, 32·3; B, 3·2%), and a residue (0·20 g.). A condensate at −80° (0·70 g.) from this distillation afforded on further distillation 1 : 4-dichlorobutane (0·55 g.), b. p. 150°/760 mm., n_D^{20} 1·4530 (Found : Cl, 55·0%). The yield of borate indicates conclusively the presence of the dichloroboronite in the condensate.

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The Order and Mechanism of the Isotopic Exchange Reactions of Secondary and Tertiary Alkyl Bromides in Anhydrous Acetone.

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Isotopic-exchange reactions between radioactive lithium bromide and *iso*propyl bromide and *tert.*-butyl bromide were studied in anhydrous acetone over a range of ionic concentrations. An equation was found according to which the first- and second-order rate constants for these reactions were determined.

The first-order contribution to the exchange reaction of *iso*propyl bromide is too small to be accurately determined. For the reaction of *tert.*-butyl bromide at 40° and a lithium bromide concentration of 0·01N, the first- and the second-order reaction contribute about equally to the exchange rate.

The frequency factors and Arrhenius energies of activation for these reactions were determined.

MANY data have been published on exchange reactions between halogen ions and alkyl halides in different solvents (for summaries, see Wahl and Bonner, " Radioactivity Applied to Chemistry," Chapman and Hall, London, 1952, p. 31; National Bureau of Standards, Circular 510, U.S. Dept. of Commerce, Tables of Chemical Kinetics, 1951, p. 279). Hughes and his co-workers used these reactions to demonstrate the mechanism of the Walden inversion (*J.*, 1935, 1525; 1936, 1173; 1938, 209). More recently this type of reaction has been used in investigating the mechanism of nucleophilic substitution reactions and making a semi-quantitative study of the effect of steric retardation (Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173; 1949, S 400; de la Mare, England, Fowden, Hughes, and Ingold, *J. Chim. phys.*, 1948, **45**, 246).

Ingold (" Structure and Mechanism in Organic Chemistry," Bell and Sons, London, 1935, p. 310) makes the fundamental postulate that a nucleophilic substitution S_N, as a heterolytic reaction in solution, normally has available two reaction mechanisms. In the case where a radioactive halogen ion undergoes exchange with the halogen atom in an alkyl halide, these mechanisms may be represented as follows :

$$\text{(i)} \qquad RX + {}^*X^- \rightleftharpoons {}^*X \cdots R \cdots X \rightleftharpoons {}^*XR + X^-$$

a bimolecular mechanism giving rise to a second-order reaction and

$$\text{(ii)} \qquad RX \rightleftharpoons R^+ + X^-$$

followed by

$$R^+ + {}^*X \rightleftharpoons R{}^*X$$

The slow step in this exchange, which determines the rate of the reaction, is the ionization of the organic halide which can be followed by a rapid combination of the alkyl ion with a radioactive bromine ion. This ionization mechanism results in a first-order reaction, the rate constant being dependent on the concentration of the organic molecule alone.

It is realized that in a homologous series of reactions, there is no abrupt change from the one mechanism to the other. In a weak ionizing solvent such as acetone the ionization mechanism is imperceptible in reactions of primary halides; hence a second-order rate law is followed, as was shown by le Roux and Sugden (*J.*, 1939, 1279; 1945, 586). On the other hand, tertiary halides react according to an ionization mechanism in a strongly

ionizing solvent such as anhydrous formic acid, as was shown by Kokoski, Thomas, and Fowler (*J. Amer. Chem. Soc.*, 1941, **63**, 2451). It is conceivable that between these two extremes there will be exchange reactions where the two mechanisms contribute in varying proportions to the overall exchange rate. The relative contributions will depend on the extent of branching in the organic molecule near the reactive carbon atom, and on the solvent used. The problem is then to determine the relative contribution of each of these mechanisms to the overall reaction in a particular solvent. This can conveniently be done by using radioactive tracers.

In the reaction $RX + M^*X \rightleftharpoons R^*X + MX$ the constant rate of exchange is given by

$$R = -[ab/t(a+b)] \ln [1 - x/c(1 + b/a)] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where a and b are the total concentrations of the alkyl and alkali halides, RX and MX, respectively. The concentrations of R^*X and M^*X are negligibly small in comparison with those of RX and MX; x/c is the ratio of the radioactivity in RX to the total radioactivity after time t.

If the exchange follows a purely second-order rate law, the constant rate of exchange is given by

$$R = k_2ab \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and when a purely first-order rate law is followed, this value is given by

$$R = k_1a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

If, however, the exchange takes place by both the bimolecular and the ionization mechanism simultaneously, giving rise to a mixed first- and second-order reaction, the rate of exchange is given by

$$R = k_1a + k_2ab$$

whence

$$R/a = k_1 + k_2b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Equation (4) is that of a straight line for the plot of R/a against b. The values of k_1 and k_2 are obtained from the intercept and gradient of this line, respectively.

When MX is a strong electrolyte in the solvent used, as is potassium iodide in acetone, the ionic concentration equals that of MX at fairly low concentrations. When MX, however, is a weak electrolyte in the solvent concerned, as is lithium bromide in acetone, the degree of dissociation of the salt in the solvent must be taken into account. Evans and Sugden (*J. Chim. phys.*, 1948, **45**, 147; *J.*, 1949, 270) showed that in the last-mentioned circumstances the reaction follows Acree's hypotheses (*J. Amer. Chem. Soc.*, 1915, **37**, 902), in which case $k_2 = k_i\alpha + k_m(1 - \alpha)$. It was found by Evans and Sugden, and confirmed by the authors, that the value of k_m is of the same order as the probable error. The actual specific rate of exchange between halide ions and alkyl halide molecules is therefore given by $k_i = k_2/\alpha$, and the rate equation for the second-order reaction becomes

$$R = k_i\alpha ab \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

On use of this second-order constant, equation (4) becomes

$$R/a = k_1 + k_i\alpha b \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

which is a straight line for the plot of R/a against αb (cf. Fig.).

Application of equation (6) to the experimental results of the reaction between bromide ions and *n*-butyl bromide in dry acetone gives a straight line passing through the origin. It shows that the first-order component of this reaction is imperceptibly small.

The order of the exchange reaction between bromine ions and *tert.*-butyl bromide in dry acetone at 40° was tested by using concentrations of lithium bromide from *ca.* 0·1N to 0·005N. The results of these experiments are summarized in Table 1. The values of α in the second column were calculated as described in the Experimental section. The last column contains values of k_i calculated according to equation (5), and the penultimate column contains the values of k_1 which is equal to R/a. It is seen that neither a first- nor a second-order rate law is followed. The plot of R/a against αb, however, gives a

straight line within the limits of the experimental accuracy. The values of k_1 and k_i calculated from these results according to equation (6) by the method of least squares are $k_1 = 32 \times 10^{-8}$ sec.$^{-1}$ and $k_i = 6{\cdot}05 \times 10^{-5}$ mole^{-1} l. sec.$^{-1}$. These values when substituted

TABLE 1. tert.-*Butyl bromide and lithium bromide* (Li*Br) *in acetone at* 40°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i
96·43	0·175	16·88	129	7·6	10·05	0·280	2·824	52	18·4
,,	,,	,,	139	8·2	,,	,,	,,	53	18·8
48·36	0·194	9·380	81	8·6	9·91	0·281	2·785	47	16·9
,,	,,	,,	91	9·7	,,	,,	,,	49	17·6
24·67	0·237	5·846	65	11·1	5·03	0·348	1·750	40	22·9
,,	,,	,,	71	12·1	,,	,,	,,	40	22·9

in equation (6) give $R/a = 32 \times 10^{-8} + 6{\cdot}05 \times 10^{-5}\alpha b$. It is seen that for values of b of the order of 0·01N, the two mechanisms contribute about equally to the exchange rate.

Experiments similar to the above were carried out with *iso*propyl bromide in acetone at 40°. The experimental results, summarized in Table 2, show from the values of k_i in the last column that there is only a 20% increase in this constant for a 10-fold change in concentration. This variation is nevertheless substantial and indicates that the exchange does not take place solely according to a second-order rate law. The rate constants calculated according to equation (6) are $k_1 = 22{\cdot}6 \times 10^{-8}$ and $k_i = 44{\cdot}3 \times 10^{-5}$. Substituted in equation (6) these values give $R/a = 22{\cdot}6 \times 10^{-8} + 44{\cdot}3 \times 10^{-5}\alpha b$. For values of b of the order of 0·01N the first-order component contributes about 5% to the rate of exchange. This value is of the same order of magnitude as the experimental error in determining the exchange rate. It is therefore probable that k_1 is even much smaller and it is clear that this method of analysing the experimental results does not give reliable values of k_1 where this is so small. This analysis nevertheless shows that there is a perceptible first-order contribution to the exchange rate and it gives more reliable values for k_2 than would have been obtained by neglecting the first-order contribution. In the case of *tert.*-butyl bromide, where the first-order contribution is much larger, reliable values of k_1 are obtained.

tert.-*Butyl bromide at* 40°.

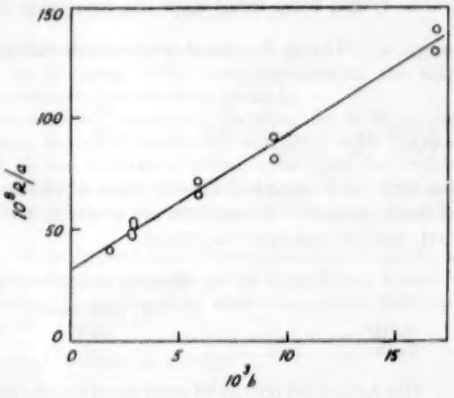

TABLE 2. iso*Propyl bromide and lithium bromide* (Li*Br) *in acetone at* 40°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^5k_i
48·36	0·194	9·380	432	46·0	10·05	0·280	2·824	147	52·0
,,	,,	,,	444	47·3	,,	,,	,,	151	53·0
24·67	0·237	5·846	278	47·6	9·81	0·282	2·767	146	52·8
,,	,,	,,	283	48·4	5·03	0·348	1·750	97	55·4
					,,	,,	,,	101	57·7

To determine the activation energies and frequency factors of these reactions, experiments were carried out at two more temperatures, the concentrations of lithium bromide ranging from 0·05 to 0·005N. The experimental results for *tert.*-butyl bromide are summarized in Tables 3 and 4 and those for *iso*propyl bromide in Tables 5 and 6.

TABLE 3. tert.-*Butyl bromide and lithium bromide* (Li*Br) *in acetone at* 20°.

10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$	10^3b	α	$10^3\alpha b$	$10^8R/a$
49·80	0·220	10·95	9·34, 9·58	19·70	0·265	5·220	6·12, 6·42	5·18	0·379	1·963	4·38, 4·60
25·40	0·253	6·425	6·63, 7·06	10·34	0·316	3·268	4·92, 5·35				

TABLE 4. tert.-*Butyl bromide and lithium bromide* (Li*Br) *in acetone at* 60°.

10^3b	α	$10^3\alpha b$	$10^3R/a$	10^3b	α	$10^3\alpha b$	$10^3R/a$	10^3b	α	$10^3\alpha b$	$10^3R/a$
46·96	0·165	7·741	560, 590	99·72	0·248	2·416	316, 325	4·88	0·307	1·500	248, 253
23·92	0·196	4·689	415, 431	9·61	0·249	2·393	340, 341				

TABLE 5. iso*Propyl bromide and lithium bromide* (Li*Br) *in acetone at* 20°.

10^3b	α	$10^3\alpha b$	$10^3R/a$	10^3b	α	$10^3\alpha b$	$10^3R/a$	10^3b	α	$10^3\alpha b$	$10^3R/a$
49·8	0·220	10·95	53·7, 55·1	10·34	0·316	3·268	17·3, 17·5	9·335	0·325	3·034	14·8
25·4	0·253	6·425	31·8, 32·5	10·05	0·319	3·206	15·6, 16·3	5·18	0·379	1·963	11·0, 11·5

TABLE 6. iso*Propyl bromide and lithium bromide* (Li*Br) *in acetone at* 60°.

10^3b	α	$10^3\alpha b$	$10^3R/a$	10^3b	α	$10^3\alpha b$	$10^3/Ra$
46·91	0·165	7·741	2447, 2466, 2512	9·70	0·248	2·410	854, 913
23·92	0·196	4·689	1586, 1624	9·46	0·250	2·367	868, 886
9·74	0·248	2·416	937, 944	9·48	0·307	1·500	640, 648

The first- and second-order rate constants were calculated for the *tert.*-butyl bromide reaction according to equation (6). Only the second-order constants of the *iso*propyl bromide reaction were calculated. The values of these constants are summarized in Table 7, and from these data the frequency factors and Arrhenius activation energies of

TABLE 7. *First- and second-order rate constants at* 20°, 40°, *and* 60°.

	10^5k_1			10^5k_1		
	20°	40°	60°	20°	40°	60°
Bu^{t}Br	3·6	32	200	0·55	6·05	48·7
Pr^{i}Br	—	—	—	4·86	44·3	295

the first- and second-order reactions of the two bromides were calculated by the method of least squares. The results are given in Table 8, the subscripts 1 and 2 referring to the first- and second-order reactions.

TABLE 8. *Arrhenius energies of activation and frequency factors.*

	E_1 (kcal./mole)	$\log_{10} A_1$	E_2 (kcal./mole)	$\log_{10} A_2$
Bu^{t}Br	19·7	7·2	21·8	11·0
Pr^{i}Br	—	—	20·0	10·6

The Arrhenius energy of activation for the *iso*propyl bromide reaction was also calculated from the experimental results by ignoring the first-order contribution and using only those values for which the ionic concentration is about 0·01N. The values so obtained are $E_a = 20{\cdot}9$ kcal. and $\log_{10} A = 11{\cdot}3$. These values differ appreciably from those obtained by the more laborious method which must, however, be considered the more accurate way of determining these quantities.

The value of 20·0 kcal. for the activation energy of the *iso*propyl bromide reaction is only 0·2 kcal. higher than the value used by Ingold (*op. cit.*, p. 408). The above value of the activation energy for the second-order reaction of *tert.*-butyl bromide is in exact agreement with the value quoted by Ingold. This is, however, only incidental, because it is not clear how the latter value was obtained (cf. de la Mare, England, Fowden, Hughes, and Ingold, *J. Chim. phys.*, **1948**, **45**, 236). Moreover, other activation energies for these bromide-exchange reactions as determined by us are about 0·8 kcal. higher than the values used by de la Mare *et al.*

TABLE 9. *Calculated values of* $K_{therm.}$.

Temp.	0°	10°	20°	25°	30°	40°	50°	60°
D	21·46	20·48	19·56	19·10	18·67	17·80	16·98	16·26
$10^4K_{therm.}$	7·07	6·52	5·52	5·02	4·83	4·23	3·48	3·18

EXPERIMENTAL

Acetone.—To pure acetone was added anhydrous magnesium perchlorate and it was left for 2 days with occasional shaking. It was then distilled from the perchlorate through a 20″

fractionating column packed with glass helices and surrounded by a vacuum-jacket, at a take-off ratio of 1 : 10. Only the middle fraction was collected for use.

Radioactive Lithium Bromide.—Radioactive bromine was obtained from Harwell in batches of 2 g. of ammonium bromide, with an activity of *ca.* 30 mc at delivery. This was dissolved in 50 ml. of water, an excess of lithium hydroxide added, and the mixture heated to convert all the bromide into lithium bromide. The impure lithium bromide was then recrystallized several times from pure, dry acetone to remove excess of lithium hydroxide and other impurities. It was finally dissolved in 100 ml. of the acetone and this was kept as the stock " active solution."

Pure lithium bromide was prepared by neutralizing the purest obtainable lithium hydroxide with hydrobromic acid solution. The product was recrystallized several times from pure acetone and finally heated to above 200° to expel all water of crystallization.

Alkyl Bromides.—The purest Eastman Kodak products were fractionated through the column described above. Only the middle portions, distilling within 0·1°, were retained. The *tert.*-butyl bromide was fractionated twice, the second time just before use. *tert.*-Butyl bromide had n_D^{20} 1·4282, and *iso*propyl bromide 1·4251.

Standard Solutions and Methods of Analysis.—All solutions were made up at 20°, and concentrations at the reaction temperatures were corrected for by using the following expression for the volume expansion of acetone :

$$V_t = V_0 (1 + 1{\cdot}324 \times 10^{-3} + 3{\cdot}809 \times 10^{-6} - 0{\cdot}8798 \times 10^{-9})$$

The concentrations of the lithium bromide solutions were determined by titration against standard silver nitrate solution with eosin as indicator. The concentrations of the alkyl bromides were determined gravimetrically by precipitation as silver bromide.

Kinetic Procedure.—The reactions were carried out essentially as done by le Roux and Sugden (*loc. cit.*). After completion of reaction the alkyl halide was extracted with benzene. The activities of the benzene solution and of the acetone solution were then determined consecutively in the same liquid-type Geiger–Müller counter tube. When corrected, the ratio of the activity of the benzene solution and the activity of the acetone solution gave the value of x/c in equation (1).

The correction factor by which x/c had to be multiplied was determined experimentally as follows. Radioactive alkyl bromide was dissolved in acetone to give the requisite molarity. It was extracted by benzene in exactly the same way as was done with the reaction mixtures. The required correction factor was then given by

$$f = \frac{\text{activity of the alkyl bromide in acetone}}{\text{activity of alkyl bromide in benzene}}$$

The value of this factor is dependent upon the molarity of the bromide, its molecular weight, density, and solubility in water, and upon the extent to which it is hydrolysed during the extraction process. These values vary from 1·027 for 0·1M-*n*-butyl bromide to 1·255 for 0·4M-*tert.*-butyl bromide.

Calculation of Degree of Dissociation.—Sugden and Evans (*loc. cit.*) calculated the degree of dissociation of lithium bromide in acetone at 25° and 65·5°, and by a slightly different method we have obtained the value $K_{\text{therm.}} = 5{\cdot}02 \times 10^{-4}$ at 25° in good agreement with their value. The degree of dissociation at any other temperature can then be calculated from Bjerrum's theory (*Kgl. Danske Videnskab. Selsk.*, 1926, **7**, No. 9) and use of standard values for the necessary coefficients (Åkerlöf, *J. Amer. Chem. Soc.*, 1932, **54**, 4125; Harned and Owen, " The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, p. 123). The values of $K_{\text{therm.}}$ so obtained, and used for the values of α shown in the Tables, are given in Table 9. It must be emphasized that the values of α obtained by the above method are only approximate and await confirmation from accurate conductivity measurements at the various temperatures.

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The Chromatography of Gases and Vapours. Part V. Partition Analyses with Columns of Silicone 702 and of Tritolyl Phosphate.*

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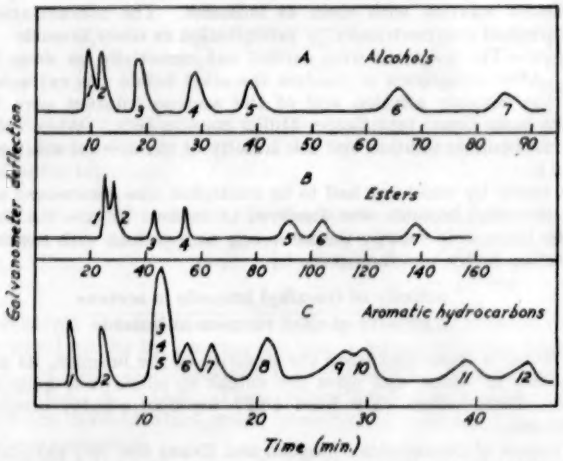
The paper describes an apparatus for partition gas chromatography. Results obtained with this apparatus for the vapours of alcohols, esters, and aromatic hydrocarbons on columns of silicone 702 fluid and of tritolyl phosphate are presented as plots of corrected retention volumes per g. of column fluid against the inverse of the column temperature.

In Part II (*J.*, 1953, 1600) an apparatus was described for the separation and analysis of mixtures of volatile substances using the partition gas chromatographic technique, originated by Martin and James (*Biochem. J.*, 1952, **50**, 679). An improved form of this apparatus has been used to record a large number of chromatograms by means of columns of Silicone 702 fluid and of tritolyl phosphate. Typical chromatograms are illustrated in Fig. 1.

Fig. 1. *Typical chromatograms.*



(*A*) 1 μl. each of seven alcohols: ethyl (1), *iso*propyl (2), *n*-propyl (3), *iso*butyl (4), *n*-butyl (5), *iso*pentyl (6), and *n*-pentyl (7). Column: 2·82 g. of Silicone 702 on 7·05 g. of Celite 535. Temp. 76·9°. Flow rate: 11·8 ml./min. at N.T.P.

(*B*) 0·7 μl. each of seven esters: methyl propionate (1), ethyl acetate (2), *iso*butyl formate (3), *n*-propy acetate (4), ethyl *iso*butyrate (5), *iso*propyl *iso*butyrate (6), *iso*propyl *n*-butyrate (7). Column: as (*A*). Temp. 77·0°. Flow rate: 11·7 ml./min. at N.T.P.

(*C*) 5 μl. each of twelve aromatic hydrocarbons: benzene (1), toluene (2), ethylbenzene (3), *m*-xylene (4), *p*-xylene (5), *o*-xylene (6), *iso*propylbenzene (7), mesitylene (8), *sec.*-butylbenzene (9), *p*-cymene (10), indene (11), *tert.*-pentylbenzene (12). Column: 1·85 g. of Silicone 702 on 4·63 g. of Celite 535. Temp. 132°. Flow rate: 27·4 ml./min. at N.T.P. (To illustrate the effect of a large sample on a column of poor separation efficiency.)

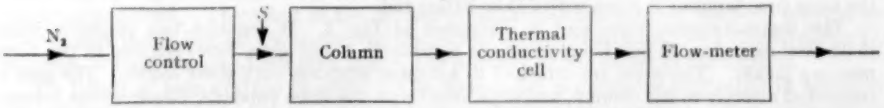
We present a summary of some of these results in a manner which, we hope, will facilitate their use by other workers. We plot our results for a series of alcohols, esters, and aromatic hydrocarbons on these two types of column in terms of " corrected retention volumes per gram " as a function of temperature. We hope that by so doing we shall help to provide a basis for a scheme of analysis using gas chromatography as an absolute method.

* Part IV, *J.*, 1954, 3446.

Experimental

Apparatus.—Fig. 2 is a block diagram of the apparatus. Nitrogen from a cylinder passes successively through the flow-control, the chromatographic column, the thermal-conductivity cell, and the flow-meter. Samples for analysis are injected at *S*.

Fig. 2. *Block diagram of apparatus.*



The flow-control is illustrated in Fig. 3. This is the device described by James and Phillips (*J. Sci. Instr.*, 1952, **29**, 362), modified to work at pressures up to 2·5 atm. Nitrogen from the cylinder enters the control through *A* at a rate greater than required for the flow through the column, and passes to the column through *B via* the capillary *C*. A constant flow is maintained

Fig. 3. *Flow control.*

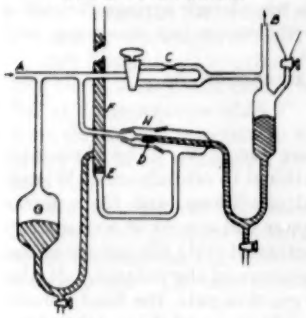


Fig. 4. *Column with vapour jacket.*

Fig. 5. *Double-cell glass thermal-conductivity unit.*

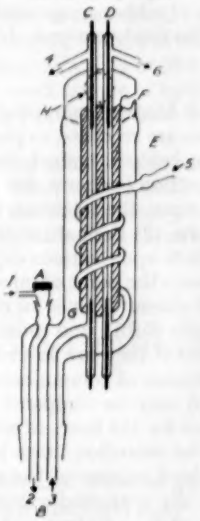


Fig. 6. *Butt-joint sample injector.*

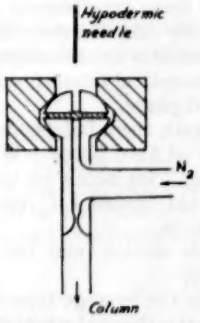


Fig. 5. Gas path indicated by arrows 1 to 6, sample injected at *A*, column sealed on at *B*, cell for measuring vapour concentration *C*, compensating cell *D*, mercury jacket *E*, mercury expansion bulb *F*, vapour jacket *G*, condenser connection *H*.

by keeping a constant head of mercury across *C*. In order to prevent too great a pressure drop from developing across the sintered-glass disc *D*, it is surrounded by a jacket *H* leading to *EFG*, a self-adjusting blow-off. By connecting the reservoir *G* to *A*, and placing the sintered-glass disc *E* about 10 cm. above the surface of mercury in *G*, a more or less constant pressure difference of 10 cm. is maintained across *D*. The by-pass below *C* is used when the nitrogen is first turned on and enables equilibrium pressures to be set up more rapidly. Part of *H* can be removed for repair or replacement of the sintered-disc valve *D*.

A typical column is illustrated in Fig. 4. It consists of a U-tube, of 5 mm. internal diameter and 1 m. long, enclosed in a vapour jacket maintained by an electrically heated boiler. For operation at the higher temperatures, the jacket is lagged with asbestos and can also be supplied with a small amount of auxilliary heating. The column is packed with about 10 g. of a mixture of Celite (535, Johns-Mansville) and the fixed liquid phase. This occupies about 75 cm. of each

arm of the U-tube. The column mixture is prepared in the following way. The Celite is size-graded by sedimentation, washed with 4N-nitric acid, then distilled water, and dried at 120°. It is then mixed with the requisite quantity of the fixed liquid phase (about 8—20 g. of Celite) and formed into a slurry with dry ether. The ether is evaporated with continuous stirring, and finally the mixture is shaken for ½ hour. The mixture is poured into the column, 0·5 g. at a time, and is shaken down by agitating the column against the spindle of an electric motor, at the same time tamping it down with a close-fitting rod.

The thermal-conductivity unit is illustrated in Fig. 5. It contains two platinum wires (0·05 mm. diameter, 14 cm. long, resistance 8 ohms) in 5-mm. glass tubes encased in the same mercury jacket. The wires are attached to tungsten supports with silver solder. The unit is connected directly to the column, and is jacketed with the same vapour. Gas from the column passes through the left-side tube, the vapours are then condensed out from the nitrogen in a dry ice-trap (not illustrated), and the nitrogen allowed to pass on through the spiral to the second compensating tube. The two wires form adjacent arms of a direct-current Wheatstone bridge, driven by a 4-v accumulator. The output of the bridge is recorded (Ether Indicorder; Ether Ltd., Birmingham).

The flow-meter consists of a capillary across a U-tube filled with liquid paraffin.

The samples are injected on to the column by means of a hypodermic syringe through a serum cap. Fig. 6 illustrates an alternative arrangement to the serum cap, consisting of a piece of rubber compressed by a butt-joint.

The dead-volume is obtained by injecting a small sample of air or hydrogen.

Discussion

(i) *Mode of expressing Results.—Corrected retention volumes per g.*, V_g. The chromatograms are recorded as plots of vapour concentration (proportional to off-balance of Wheatstone bridge) against time. Under constant experimental conditions, and for a linear absorption isotherm, the peak maximum for a particular vapour will appear at a characteristic time, the retention time. This retention time is a function of: (1) the nature of the vapour, (2) the nature of the fixed phase, and (3) the temperature of the column. It also depends upon various experimental parameters, such as the gas-flow rate, the dead volume between the point of injection and the thermal conductivity detector, and the weight of the fixed phase. Values for retention times are therefore only of relative importance [see p. 1486, Results (i)(b)], and must be corrected to eliminate the effects of these experimental parameters if they are to provide results which can be used directly by other workers for the prediction of column behaviour and as a basis for a scheme of absolute identification, and which may be compared among themselves to give results of theoretical interest, such as values for the heats of solution of the vapours in the column fixed phase.

Our retention times have therefore been corrected so as to make them independent of the dead volume of the apparatus, the flow rate, and the weight of fixed phase. We call the fully corrected values "corrected retention volumes per gram," for which we use the symbol V_g. Values of V_g (on a logarithmic scale) are then plotted against $1/T$, where T is the column temperature. Such plots approximate to straight lines.

(ii) *Correction Procedure.*—The procedure is outlined in this section, and the next section gives an example worked out in detail.

(a) *Correction for dead volume.* The retention time represents the average time taken for a molecule of the vapour to pass from the injection point to the thermal conductivity cell. This time consists of two parts, the time spent in the gas phase, and that spent in the fixed phase. We are only interested in the second part; the first part depends upon the dead volume of the apparatus [which includes the volumes of the tubes leading from the injection point to the column and from the column to the thermal-conductivity cell (about 7 ml.), and the volume of the gas phase in the column (about 20 ml.)] and the flow rate. It is most simply determined by measuring the time taken for a small sample of air or hydrogen (whose absorptions in the fixed phase are sufficiently small to be neglected) to pass to the thermal conductivity cell after injection. This time is usually relatively small.

(b) *Correction for flow rate.* For a given column, the time which a vapour spends in the fixed phase will be inversely proportional to the flow rate of gas by which it is being removed. The time spent in the fixed phase is therefore multiplied by the flow rate to give the retention

volume. The flow-rate correction is complicated, however, by the fact that the gas flowing through the column is a fluid whose volume changes with both pressure and temperature.

(1) Effect of pressure changes. The flow-meter is calibrated in terms of volumes of gas delivered at atmospheric pressure. The pressure at the outlet of the column will be slightly higher, by virtue of the pressure drop across the flow-meter, and at the inlet of the column considerably higher, because of the pressure drop across the column. Two corrections are therefore required. The effect of the pressure drop across the column has been treated by Martin and James (*loc. cit.*), who derived the correcting factor $2[(p_1/p_0)^3-1]/3[(p_1/p_0)^2-1]$, where p_1 is the pressure at the inlet and p_0 the pressure at the outlet of the column.

(2) Effect of temperature changes. The flow-meter is normally calibrated in terms of the volume of gas delivered at a temperature near room temperature. For convenience we have calibrated our flow-meter in terms of gas at 0°. The gas, however, passes through the column at the temperature of the column T, and the flow-meter value must be multiplied by $T/273$ to give the real volume of gas passing through the column. But as the temperature is to be one of the variables it is not essential to apply a temperature correction, and we have therefore omitted it.

(c) *Correction for weight of fixed phase.* The retention volume obtained as above is divided by the weight of fixed phase to give V_g.

(iii) *Example of Correction Procedure.*—To illustrate the application of the various correction terms we take the case of methyl propionate vapour passed through a column of Silicone 702 at a temperature of 56·2°. Measurement of the recorder chart gave a time of 58·2 min. from the time of injection to the peak maximum. Injection of a small sample of hydrogen under the same conditions gave a time of 2·7 min. The corrected retention time is thus 55·5 min.

The flow rate as determined by the flow-meter was 11·0 ml. of nitrogen per min. at N.T.P. This gives an uncorrected retention volume of 610 ml. The pressure at the inlet of the column was 123·0 cm. (of Hg), at the outlet 78·1 cm., and the atmospheric pressure was 76·0 cm. The correction factor for the pressure drop across the column is therefore

$$\frac{2}{3}\cdot\frac{(123{\cdot}0/78{\cdot}1)^3-1}{(123{\cdot}0/78{\cdot}1)^2-1}=0{\cdot}765$$

and for the pressure drop across the flow meter 76·0/78·1. The weight of Silicone 702 in the particular column was 2·82 g. The value for V_g is thus

$$610\times 0{\cdot}765\times\frac{76{\cdot}0}{78{\cdot}1}\times\frac{1}{2{\cdot}82}=161\text{ ml.}$$

(iv) *Significance of* V_g *Values.*—If a particular vapour is equilibrated between gas and 1 g. of the fixed phase so that it is 50% in the gas phase and 50% in the fixed phase, then V_g will be the volume of gas (corrected to 0° at constant pressure); V_g is thus related to α, the partition coefficient defined by the equilibrium relation

$$\alpha=\frac{\text{Weight of vapour per unit volume of fixed phase}}{\text{Weight of vapour per unit volume of gas}}$$

by the equation $V_g=273\rho\alpha/T$, where ρ is the density of the fixed phase. Alternatively we may express V_g as the volume of gas (measured at 0°) which has passed through a hypothetical ideal column, containing 1 g. of fixed phase, when the peak maximum emerges. This ideal column has a constant pressure (equal to the pressure at which the volume of gas is measured) throughout, and zero dead-volume.

We express our results in terms of V_g rather than in terms of α, in order to simplify the correction procedure. If we had divided our retention volumes by the volume of the fixed phase, instead of by the weight, then we should have eliminated the density from the relation between V_g and α. However, such a procedure would require a new factor for a particular column for each temperature. Moreover, we should need to know the temperature coefficient of expansion of the fixed phase. The variation of density with temperature

enters into the calculation of heats of solution [Results (iv), p. 1488] but it gives rise to a relatively small correction, which can be inserted directly as a small constant heat value for a particular column fluid.

The factor $273/T$ in the relation between V_g and α would disappear if we measured our retention volumes at the column temperature instead of at 0°. This, however, would complicate the correction procedure. Furthermore, omission of this factor enables heats of solutions to be calculated more directly [see Results (iv), p. 1488], as it is equivalent to expressing our results in terms of Bunsen's coefficient instead of Ostwald's coefficient (α).

Results

The corrected retention volumes per g. for series of esters, alcohols, and aromatic hydrocarbons have been determined over a range of temperatures for columns of silicone 702 fluid, and of tritolyl phosphate. These values are presented in Figs. 7, 8, 9, and 10 as plots of $\log_{10} V_g$ against $1/T$. The slopes of these plots are related to the heats of solution of the vapours [see

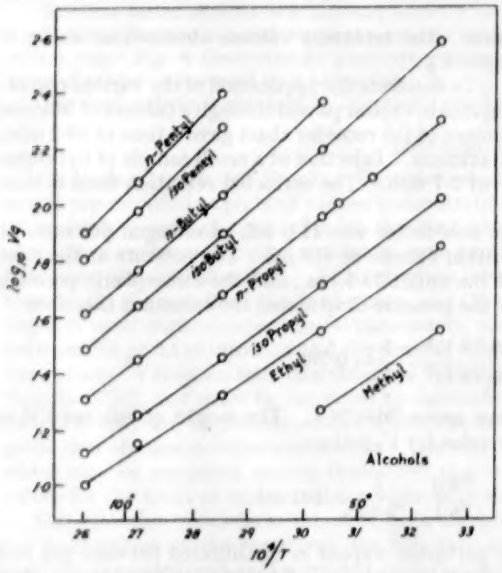


FIG. 7. Log_{10} V_g *values (corrected retention volumes per g.) for alcohols on Silicone* 702 (Midland Silicones Ltd.).

Results (iv), p. 1488]. The plots prove to be straighter than might have been supposed, in view of the normal variation of heats of solution with temperature. From the plots, values of V_g may be read off for any temperature in the range. The plots can be used both analytically, to interpret and predict column behaviour, and theoretically, to deduce values for heats of solution.

(i) *Use of* V_g *values for Vapour Identification.*—When a chromatogram has been recorded, each peak is assigned its appropriate V_g value, by using the correction procedure given above. For one chromatogram this will mean multiplying each retention time by one constant. The vapours corresponding to each peak can then be identified by reference to a complete set of plots, as with a set of melting or boiling points. The identification can be checked by running the same sample at a different temperature or on a different column.

The validity of such a procedure clearly depends upon the reproducibility of the V_g values. In order to gain some idea of this, we have repeated many of our results on different columns composed of the same fixed phase. Examples are given in the next section. In general, we feel that the results which we have plotted are reliable to $\pm 4\%$, which corresponds to 0·02 log unit. This accuracy is quite sufficient for most purposes, but it can be increased to $\pm 1\%$ by use of the method of internal standards [see (b), p. 1485].

(a) *Reproducibility of* V_g *values.* (1) Effect of repacking the column. A column containing Silicone 702 as fixed phase was packed to give a total length of 142·4 cm. A mixture of methyl

acetate, ethyl acetate, methyl propionate, and benzene was chromatographed. The column was then shaken out, and repacked in the same tube to approximately the same density as before. Its length was now 141·6 cm. The same mixture was chromatographed on this column. Finally, the column was again shaken out and repacked very tightly, so that its length was 107·0 cm. A third chromatogram of the mixture was recorded. In each case the column was jacketed at 77°. The V_g values obtained in these three experiments are given in Table 1.

TABLE 1. *Effect of repacking column on reproducibility of* V_g *values.*

Column length (cm.)	142·4	141·6	107·0
		V_g Values	
Methyl acetate	33·9	32·8	33·3
Ethyl acetate	68·5	67·1	68·0
Methyl propionate	78·7	76·3	78·0
Benzene	102·0	99·5	100·7

FIG. 8. V_g *Values for aromatic hydrocarbons and esters on Silicone* 702.

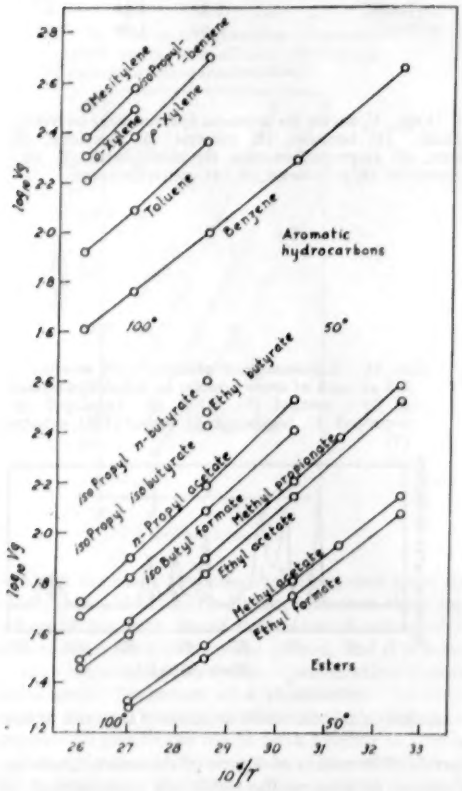
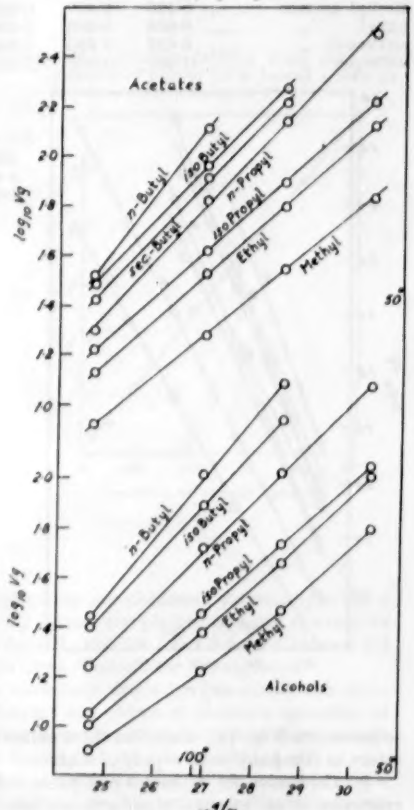


FIG. 9. V_g *Values for acetates and alcohols on tritolyl phosphate.*



(2) Use of different samples of fixed phase. Two columns were constructed with different samples of Silicone 702 fluid (Batch Nos. EE 44 and EE 67, supplied by W. Edwards and Co.). Values of V_g obtained with these two columns are given in Table 2.

(b) *Use of an internal standard.* While a reproducibility of about ±4% can be expected in experiments performed with different columns, the results obtained on one column are more reproducible. The variation in these results will arise from slight variations of column temperature, flow rate, and injection procedure. The effect of these can be very much reduced by

using a substance as an internal standard. Table 3 gives, for example, the retention times for a series of esters on a column of tritolyl phosphate, the retention time of *n*-propyl acetate being used as the standard. The first two columns contain values given by mixtures containing all

TABLE 2. V_g *Values obtained with two samples of Silicone* 702 *fluid.*

	Sample EE 44	Sample EE 67		Sample EE 44	Sample EE 67
	Columns at 77°			Columns at 35°	
Benzene	101	100	Methyl acetate ...	140	141
Toluene	237	229	Methyl propionate	393	387
p-Xylene	512	503	Ethyl alcohol ...	66·2	72·0
Methyl acetate ...	33·9	35·6	*iso*Propyl alcohol	101	105
Ethyl acetate	68·5	69·0	*n*-Propyl alcohol	196	200
Methyl propionate	78·7	79·7	Ether	78·4	82·0
n-Butyl alcohol ...	104	109			

TABLE 3. *Use of an internal standard : retention times relative to* n-*propyl acetate.*
(Column of tritolyl phosphate at 98°).

Methyl acetate	0·426	0·427	0·420	*sec.*-Butyl acetate	1·17	1·16	1·16
Ethyl ,, ...	0·605	0·606	0·606	*iso*Butyl ,, ...	1·32	1·31	1·31
*iso*Propyl ,, ...	0·683	0·685	0·690	*n*-Butyl ,, ...	1·82	1·80	1·81
n-Propyl ,, ...	(1·00)	(1·00)	(1·00)				

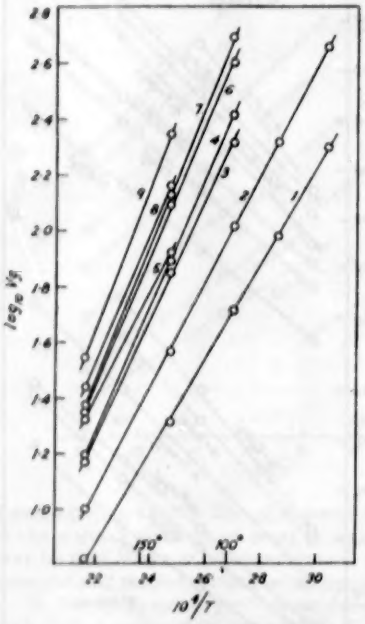
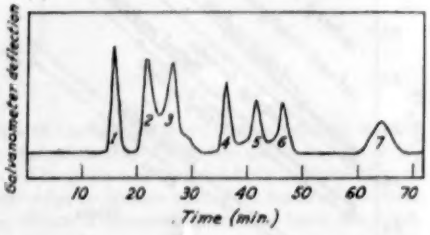


FIG. 10. Log_{10} V_g *values for aromatic hydrocarbons on tritolyl phosphate :* (1) benzene, (2) toluene, (3) *p*-xylene, (4) *o*-xylene, (5) *iso*propylbenzene, (6) mesitylene, (7) *sec.*-butylbenzene, (8) *p*-cymene, (9) *tert.*-pentylbenzene.

FIG. 11. *Chromatogram obtained with mixture o* 0·5 *µl. each of seven acetates on tritolyl phosphate at* 98° : methyl (1), ethyl (2), *iso*propyl (3), *n*-propyl (4), *sec.*-butyl (5), *iso*butyl (6), *n*-butyl (7).



seven esters (Fig. 11), while the third column contains values obtained separately for each of the esters in company with *n*-propyl acetate.

(c) *Correction for asymmetry of peaks.*—Reproducible values of V_g, or of retention times by reference to an internal standard, are only obtained so long as the peaks are symmetrical or nearly so. If the column is overloaded (so that the isotherms become non-linear), asymmetric peaks are produced with diffuse fronts and sharp tails, and the value for the peak maximum rises with the quantity of vapour. The beginnings of these peaks, however, prove to be reasonably reproducible, and by an empirical procedure in which the time between the peak maximum and the end of the peak is added to the time for the beginning of the peak (equivalent to turning the peak back to front), a good value for the symmetric peak retention time can be obtained. Thus even an asymmetric peak may be identified. Table 4 provides an illustration. The results obtained by using the empirical correction procedure are given in the last column.

(d) *Extrapolation of* V_g *values.* A complete scheme of identification would require a knowledge of V_g values for all possible vapours. It is to be hoped that in the course of time something approximating to such a complete set of values will become available from the results of a number of workers. It is, however, often possible to obtain a very good estimate for V_g values by appropriate extrapolation. Thus, Fig. 12 illustrates the relation between values of $\log_{10} V_g$ and the number of carbon atoms for a series of *n*-alcohols. It will be seen that, except for the lowest member (methyl alcohol), the values lie on good straight lines. Similar results are

TABLE 4. *Correction for asymmetry of peaks.* Values (in min.) for the retention time of ethyl acetate on a column of silicone 702 (1·85 g.). Nitrogen flow rate 20·6 ml./min. Column at 56°.

Quantity, μl.	Peak maximum	Peak beginning	Corrected peak max.	Quantity, μl.	Peak maximum	Peak beginning	Corrected peak max.
2·5	19·8	18·4	19·8	10	20·7	18·2	19·6
5	19·7	18·4	19·7	20	21·5	18·0	19·7
10	20·7	18·2	19·7	40	22·8	17·9	19·3

FIG. 12. V_g *Values as a function of number of carbon atoms for* n*-alcohols on Silicone* 702 *column at three temperatures.*

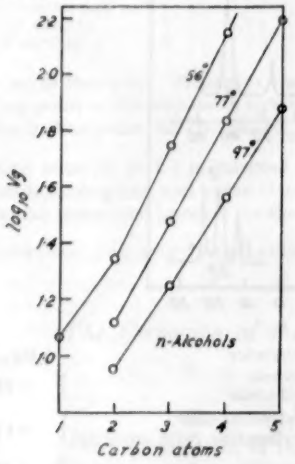
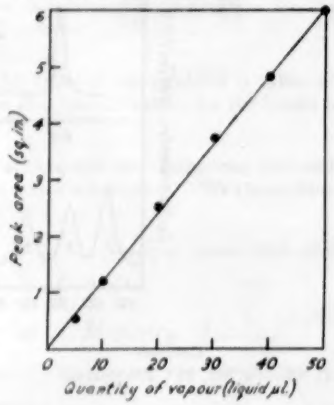


FIG. 13. *Relation between peak area and quantity of vapour for* n*-propyl acetate on a Silicone* 702 *column at* 77°.



obtained for other homologous series, and good straight lines are obtained, for example, for a whole series of aromatic hydrocarbons if their $\log_{10} V_g$ values are plotted against number of carbon atoms with use of the empirical rating of 1·0 for CH_3, 0·8 for CH_2, 0·4 for CH, and 0·2 carbon atom for a quaternary carbon, and if 0·2 carbon atom is added for *ortho*-groups.

(ii) *Quantitative Analyses.*—Quantitative analyses have been made by measuring the areas under peaks by means of a planimeter. Linear relations are obtained between quantity of vapour and peak area, as illustrated by Fig. 13. Our recorder did not have a fast enough response to justify the use of peak heights as Ray has done (*J. Appl. Chem.*, 1954, **4**, 21).

(iii) *Efficiency of Separations.*—The separative ability of a column may be expressed in terms of the number of theoretical plates. This can be calculated from the recorded chromatograms by measurement of the height of a peak h, its area a, and its retention distance l, and use of the formula

$$\text{Number of plates} = 2\pi(hl/a)^2$$

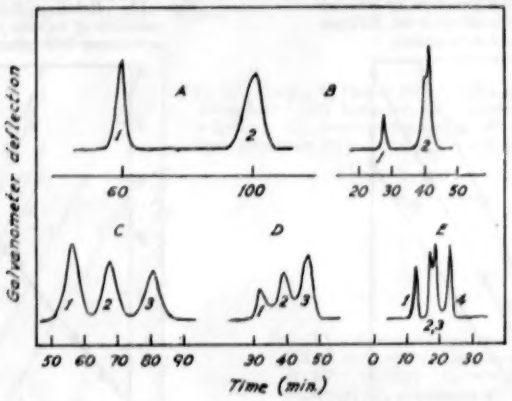
which is equivalent to Martin and Synge's method I (*Biochem. J.*, 1941, **35**, 1358). The values obtained for our columns vary considerably, but average values are 1000 for the silicone column, and 700 for the tritolyl phosphate column.

The efficiency of a column increases as the quantity of vapour is reduced. Thus on a

particular column of Silicone 702 (containing 1·82 g. of silicone) at 56°, the peak for 10 μl. of ethyl acetate corresponded to 560 theoretical plates, for 5 μl. 840 theoretical plates, and for 2·5 μl. 1100 theoretical plates. The efficiency also increases with retention volume, though this is in part due to the rather slow response of our recording system.

As the column temperature is raised, the efficiency is found to remain more or less constant for a given retention volume. Thus for the Silicone column described on p. 1481, values of $\log_{10} V_g$ (see Figs. 7 and 8) near 1·9 correspond to about 800, values near 2·2 to about 1300 and near 2·6 to about 2000 theoretical plates. If follows, therefore, that for any particular vapour the effective number of theoretical plates in a given column will increase as the temperature is reduced. Thus on a tritolyl phosphate column, the following theoretical plate values (number of plates at 105°, number of plates at 56°, ratio of number at 56° to number at 105°) were calculated; methyl acetate (200, 600, 3·0), ethyl acetate (265, 960, 3·6), benzene (360, 1410, 3·9), propyl acetate (710, 1910, 2·7). There are also differences between different classes of compounds. For example, on Silicone 702 columns, values for esters are always considerably higher than values for alcohols and aromatic hydrocarbons of comparable retention volumes.

FIG. 14. *Chromatograms to illustrate dependence of separation efficiency on number of theoretical plates and on differences* (Δ) *in the values of* $\log_{10} V_g$.



Column	Substance	Δ $\log_{10} V_g$
(*A*) Silicone 702, 35°, 1500 plates	(1) *cis*-Dichloroethylene (2) *trans*-Dichloroethylene	0·23
(*B*) Silicone 702, 157°, 800 plates	(1) 1 : 2-Di-*n*-propyl*cyclo*hexane (2) 1 : 2-Di-*n*-propylbenzene (with impurity)	0·17
(*C*) Silicone 702, 111·4°, 1500 plates ...	(1) *p*-Xylene (2) *o*-Xylene (3) *iso*Propylbenzene	0·08 0·08
(*D*) Tritolyl phosphate, 157°, 650 plates	(1) Aniline (2) *N*-Methylaniline (3) Di-*N*-methylaniline	0·09 0·07
(*E*) Silicone 702, 132°, 600 plates	(1) *iso*Butyl *iso*butyrate (2) *iso*Butyl *n*-butyrate (3) *iso*Pentyl propionate (4) *n*-Butyl *n*-butyrate	0·05

In order to illustrate the relations between separation, difference in values of $\log_{10} V_g$, and the number of theoretical plates, some chromatograms are given in Fig. 14. The relation between separation and number of theoretical plates is shown in particular by a comparison of chromatograms *C* and *D* ($\log_{10} V_g$ differences 0·08), and of chromatogram *E* (*iso*butyl *n*-butyrate and *iso*pentyl propionate, $\log_{10} V_g$ difference 0·05, 600 plates) with the separation of *iso*propyl *iso*butyrate and ethyl *iso*butyrate in Fig. 1 ($\log_{10} V_g$ difference 0·05, 2500 plates).

(iv) *Heats of Solution.*—The heat of solution, ΔH, of a vapour in the fixed phase of the column will be given by the relation

$$(\mathrm{d} \ln c/\mathrm{d}T)_p = \Delta H/\boldsymbol{R}T^2$$

where c is the concentration of vapour in the liquid at constant vapour pressure. Now $\mathrm{d}\ln\alpha/\mathrm{d}T$ is equal to $\mathrm{d}\ln c/\mathrm{d}T$ at constant weight of vapour per gas volume. Therefore

$$\mathrm{d}\ln\alpha/\mathrm{d}T = (\mathrm{d}\ln c/\mathrm{d}T)_p + (\mathrm{d}\ln p/\mathrm{d}T)_v$$
$$(\mathrm{d}\ln c/\mathrm{d}T)_p = \mathrm{d}\ln(\alpha/T)/\mathrm{d}T$$

Since $V_g = \rho\alpha 273/T$, it follows that

$$\mathrm{d}\ln V_g\rho/\mathrm{d}T = \Delta H/\boldsymbol{R}T^2$$
$$\Delta H = -2{\cdot}3\boldsymbol{R}\,[\text{Gradient}] + \boldsymbol{R}T^2\,\mathrm{d}\ln\rho/\mathrm{d}T$$

where [Gradient] is gradient of plot of $\log_{10} V_g$ against $1/T$.

The last term can be calculated from the cubical expansion coefficient of the column liquid. Values for this coefficient are 0·00083 for Silicone 702 fluid, and 0·0012 for tritolyl phosphate. The corresponding terms are −0·16 and −0·23 kcal. (the negative sign indicating a numerical increase in the value of the heat of solution). Table 5 gives a series of heats of solution calculated in this way. Wherever the plots are curved the value of the gradient is taken at the boiling point of the vapour in question. In Table 5 are also quoted values for the latent heats at the boiling point, for comparison.

TABLE 5. *Heats of solution of vapours* (in kcal./mole).

Vapour	Heat of solution in tritolyl phosphate	Heat of solution in Silicone 702	Latent heat of evapn. at b. p.	Vapour	Heat of solution in tritolyl phosphate	Heat of solution in Silicone 702	Latent heat of evapn. at b. p.
Ethyl alcohol ...	8·1	5·9	9·3	Propyl acetate	9·0	8·4	8·1
Propyl alcohol...	9·4	7·0	9·9	Benzene	8·2	7·4	7·4
Methyl acetate	7·7	7·1	7·3	Toluene	9·0	7·9	8·1
Ethyl acetate ...	8·3	7·8	7·8				

One of us (A. B. L.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant, and to the Harmsworth Trust for a senior scholarship. We thank Imperial Chemical Industries Limited for the loan of a recorder.

INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, October 26th*, 1954.]

The Capacity of the Double Layer at a Mercury Anode.

By S. E. S. EL WAKKAD and T. M. SALEM.

[Reprint Order No. 5903.]

The development of the procedure for studying the anodic oxidation of metals at very low current density enables the capacity of the double layer at a mercury anode to be readily determined by the direct method and use of a special cell and constant current unit. No previous work on mercury from the present standpoint has been published. By using a mercury electrode of large surface area and very small currents (of the order of 10^{-7} A/sq. cm.) a considerable time is required for the charging of the electrode–solution interface so that it can conveniently be followed with a valve voltmeter. The results have been confirmed oscillographically and are shown to accord with theory.

IN a series of papers (El Wakkad and Emara, *J.*, 1952, 461, 1953, 3504, 3508; El Wakkad and Shams El Din, *J.*, 1954, 3094, 3098; El Wakkad, Shams El Din, and El Sayed, *J.*, 1954, 3103) on the anodic oxidation of metals at very low current density, the true surface areas of the anodes were determined from the value of the capacity of the anodic double layer before oxide formation. The value of the capacity of the anodic double layer was always taken to be 100 μF per true sq. cm. as estimated from correlation between the work of Hickling and of El Wakkad and Emara. No previous verification for this value has been published. The development of this procedure then used enables the capacity of the double

layer at a mercury anode to be readily determined by the direction method and use of a special cell and constant current unit. By using a mercury electrode of large surface area and a very small current, the time required for the charging of the electrode–solution interface is such that it can be followed with a valve voltmeter. The results have also been confirmed oscillographically. This value has also been deduced theoretically and the result agrees satisfactorily with the experimental results.

Experimental

The Direct Potentiometric Method.—The circuit used in obtaining the variation of the potential of the mercury anode with the quantity of electricity passed employed a pentode valve as a constant-current device, so the current passing was largely independent of changes in the back e.m.f. of the electrode system. The current was supplied from a 120-v dry battery.

The electrolytic cell used was of Pyrex glass without any rubber connections. There were no greased ground joints on taps in contact with the solution. The joints were water-sealed, a thin film of conductivity water being between the two parts of the joint. The anodic compartment was a mercury pool, with a surface area of 22·9 sq. cm., connected to the electrical circuit through platinum contact. The mercury used was prepared as described by El Wakkad and Salem (*J. Phys. Chem.*, **1950**, **54**, 1371). The mercury obtained during the last distillation was introduced directly into the cell. The cathode compartment was fitted with a tight ground joint into the anode compartment and was placed in such position with regard to the anode as to ensure uniform distribution of the polarising current at the anode surface. The cathode was a platinum spiral wire. Two side tubes were for gas inlet and exit, the latter being fitted with a Bunsen valve. Measurements were carried out in 0·1M-sodium hydroxide prepared from conductivity water and "AnalaR" solid. The solution in the cell was boiled before use and cooled in an atmosphere of pure nitrogen. The currents used were 2 and 4 microamp. per electrode (*i.e.*, the current densities were $8{\cdot}7 \times 10^{-6}$ and $1{\cdot}74 \times 10^{-7}$ A/sq. cm.). In each measurement the mercury was first made cathodic to ensure the reduction of any oxide already present on the surface of the electrode (*idem, ibid.*). The current was then reversed and the potential of the anode was recorded with the help of a valve voltmeter (Electronic Instruments, England).

During the first minute from the moment of reversing the current to start the anodic pulse, the potential of the mercury electrode changed very rapidly from the very negative value (hydrogen evolution) towards the positive anodic value. The changes in potential during this minute, which are largely due to the decay of the hydrogen over-voltage, were neglected, and the potentials were recorded only during the build-up of the anodic double layer before oxide formation (El Wakkad, *et al.*, *locc. cit.*).

The reference half-cell was a saturated calomel electrode prepared according to Harned and Owen ("The Physical Chemistry of Electrolytic Solutions," **1943**, p. 32). All experiments were carried out at room temperature, 25° ±1°.

The Cathode-ray Oscillographic Method.—The circuit used was on the same principle as that used by Hickling (*Trans. Faraday Soc.*, **1945**, **41**, 333; **1946**, **42**, 518; see also Hickling and Spice, *ibid.*, **1947**, **43**, 762; Hickling and Taylor, *Discuss. Faraday Soc.*, **1947**, **1**, 277; *Trans. Faraday Soc.*, **1948**, **44**, 762; El Wakkad and Hickling, *ibid.*, **1950**, **46**, 820; El Wakkad and Salem, *J. Phys. Chem.*, **1952**, **56**, 621; El Wakkad and Hickling, *ibid.*, 1953, **57**, 203); it records the variation of potential with the quantity of electricity passed. A slight modification was necessary to make the circuit suitable for the present study: the cathode follower circuit was employed to transfer the voltage across the series of condensers to the X deflection plates of the cathode-ray tube without taking any current from the condenser. The grid anodic voltage was decreased from 360 to 240 v, and thus the sensitivity was increased. The single-sweep technique was adopted to get the necessary charging curves. The electrolytic cell used was similar to that employed in the direct potentiometric method, but the mercury anode was of 0·60 sq. cm. area. The cathode was a platinum spiral of approximately 0·5 sq. cm. in area. Observations were made in an atmosphere of pure nitrogen in 0·1M-sodium hydroxide. In each experiment the mercury electrode was first polarised cathodically for ~20 sec., the current was then switched off for ~30 sec., and the anodic polarisation was started. Two polarising currents were used, *viz.*, 15 and 45 μA per electrode. The capacity of the condenser in the circuit was 2 μF. All experiments were carried out at room temperature, 25° ±1°.

A specimen from the results obtained is shown as an oscillogram (Fig. 1, reproduced from a photograph) in which the ordinate represents potentials and the abscissæ are proportional to

the quantity of electricity passed. Suitable horizontal reference lines at intervals of 0·25 v were photographed immediately after the polarisation track so that significant potential can be read directly from the oscillograms. The quantity of electricity passed at any stage in the polarisation is obtained from the known capacity of the condenser used (which was 2 μF) in the circuit and the horizontal displacement, which is governed by the voltage to which the condenser is charged. Suitable vertical lines at intervals of 10-volt are shown to enable the quantity of electricity passed during the polarisation process to be calculated.

FIG. 1.

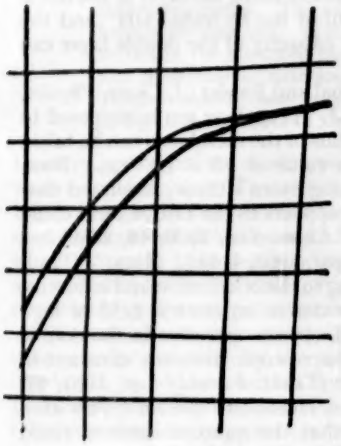
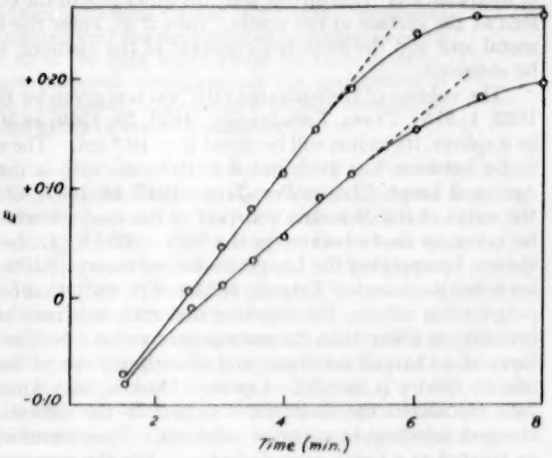


FIG 2.



RESULTS AND DISCUSSION

In Fig. 2, the lower curve is the characteristic charging curve (obtained by the direct potentiometric method) of the mercury anode with a polarising current density of $8{\cdot}7 \times 10^{-8}$ A/sq. cm. in 0·1M-sodium hydroxide. The upper curve is obtained with a polarising current density of $1{\cdot}74 \times 10^{-7}$ A/sq. cm. in the same solution. From the slopes of the two curves showing the change in potential as a function of the quantity of electricity passed, the capacity is found to be $c = 105$ and 127 μF per sq. cm. with polarising currents of $8{\cdot}7 \times 10^{-8}$ and $1{\cdot}74 \times 10^{-7}$ A per sq. cm., respectively.

Fig. 1 gives the characteristic charging curves obtained with the cathode-ray oscillography in 0·1M-sodium hydroxide with polarising currents of 15 and 45 μA/sq. cm. and a condenser of 2 μF. From the known capacity of the condenser in the circuit, *viz.*, 2 μF, and the horizontal displacement which is governed by the voltage to which the condenser is charged as shown by the vertical lines at intervals of 10 v, the quantity of electricity passed in the linear part of the curve of Fig. 1 for 0·25 v change in the potential of our mercury anode was found to be 14·7 μ coulomb with a polarising current of 45 μA. This gives a capacity of 98 μF/sq. cm. For a polarising current of 15 μA the results also give a capacity of 98 μF/sq. cm. In the Table are shown the results obtained for the capacity of the double layer on the mercury anode as obtained by the direct potentiometric method and with the cathode-ray oscillograph.

Method	Polarising c.d., A	Capacity of double layer, μF/sq. cm.
Direct	$8{\cdot}7 \times 10^{-8}$	105
„	$1{\cdot}74 \times 10^{-7}$	127
Cathode-ray oscillograph	$2{\cdot}5 \times 10^{-6}$	98
„ „	$7{\cdot}5 \times 10^{-6}$	98
		Mean 107

From these results it is clear that the value taken by El Wakked *et al.* (*locc. cit.*), *viz.*, 100 μF, for the capacity of the anodic double layer from the correlation between their work and that of Hickling is reasonable.

The value of the capacity of the anodic double layer can also be obtained theoretically as follows: We can regard the double layer formed during the polarisation of an anode to be simply of Helmholtz type. The capacity per unit area is given by

$$c = D/4\pi d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where D is the dielectric constant of the medium between the layers and d is the distance between them. According to such a picture the anodic double layer will consist of a layer of hydrated OH^- ions on one side, the other side of the condenser being the layer of the metal ions at the surface of the anode; then if we know the radii of the hydrated OH^- and the metal ions and the dielectric constant of the medium, the capacity of the double layer can be obtained.

The volume of the hydrated OH^- ion was given by Bernal and Fowler (*J. Chem. Physics*, 1933, **1**, 515; *Trans. Faraday Soc.*, 1933, **29**, 1049) as 30 Å^3. If such an ion is supposed to be a sphere, its radius will be about 3×10^{-8} cm. The radius of the metal ions can be taken to be between 1×10^{-8} and 2×10^{-8} cm. with a mean value of $1{\cdot}5 \times 10^{-8}$ cm. Now, Agar and Liopis (*Anales Fis. Quim.*, 1947, **43**, 1087), utilizing Stern's theory, assumed that the value of the dielectric constant of the medium which appears in the Debye term could be taken as that of water in the bulk. Webb (*J. Amer. Chem. Soc.*, 1926, **48**, 2589) has shown, by applying the Langevin–Debye theory (*J. Physique*, 1905, **4**, 648; Marx, "Handbuch der Radiologie," Leipzig, 1925, **6**, 618, 680), that owing to the orientation and inductive polarisation effects, the effective dielectric constant of water in an electric field of high intensity is lower than its macroscopic value. Similar effects are operative in the double layer at a charged interface, and accordingly use of the macroscopic dielectric constant in Stern's theory is invalid. Conway, Bockris, and Ammar (*Trans. Faraday Soc.*, 1951, **47**, 756) calculated the dielectric constant in the diffuse and Helmholtz double layers at a charged interface in aqueous solutions. They assumed that the aqueous medium could be treated as a continuous dielectric. For the purpose of the calculation for aqueous acid solutions, they considered that the thickness of the Helmholtz layer would approximate to the radius of the hydroxonium ion, *i.e.*, about 1·55 Å.

According to Grahame (*Chem. Rev.*, 1947, **41**, 441), hydration in the Helmholtz layer is unlikely to be greater than the primary solvating water molecule in the case of the proton; since, moreover, the dielectric constant at the outer plane of the Helmholtz double layer was found to vary between 8·15 and 23 for the cathodic double layer, where one side of the double layer was mainly formed by hydroxonium ions, one is bound to consider the Helmholtz anodic layer as formed of OH^- ions hydrated with one hydration sheath.

The radius of the hydrated OH^- ion was shown before to be 3×10^{-8} cm. The value of the dielectric constant at the outer plane of the Helmholtz double layer as obtained from the calculations of Conway, Bockris, and Ammar (*loc. cit.*) lies between 34 and 38. Substituting these values in equation (1), we obtain for the capacity of the anodic double layer values lying between 100·2 and 111·9 μF per sq. cm., in good agreement with the value found experimentally.

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Adsorption on Charcoal from Aqueous Solutions of Fatty Acids: a Further Interpretation of Traube's Rule.

By A. Blackburn and J. J. Kipling.

[Reprint Order No. 5905.]

The adsorption by charcoal from aqueous solutions of formic, acetic, propionic, and *n*-butyric acids severally has been studied over the complete concentration range. The adsorption isotherms for the individual components have been obtained. It is suggested that the same type of hydrogen-bonding occurs in the adsorbed phase as in the bulk liquid phase for these systems, and molecular orientations are proposed which explain the application of Traube's rule to these systems. The formic acid system is slightly anomalous, owing to the absence of an alkyl group in the acid molecule.

In early investigations of adsorption from liquids, aqueous solutions of various fatty acids were frequently used (Freundlich, "Colloid and Capillary Chemistry," Methuen, London, 1926), though the experiments were usually confined to very low concentrations. Results recently reported (Blackburn and Kipling, *J.*, 1954, 3819) suggest that these systems, in which extensive hydrogen-bonding can take place between acid and acid, water and water, and acid and water molecules, might be among the most complicated of binary systems to investigate, and were quite unsuited to early studies in the subject.

We have shown that adsorption from non-interacting systems on charcoal is essentially unimolecular and that for the interacting system pyridine–water, the effect of hydrogen-bonding is to add one further layer to the adsorbate (Kipling and Tester, *J.*, 1952, 4123; Blackburn and Kipling, *loc. cit.*). It was therefore of interest to discover whether any relatively simple interpretation would be possible of the adsorption from aqueous solutions of acids over the entire concentration range.

Discussion.—Fig. 1 shows the isotherm of concentration change for adsorption on charcoal from aqueous solutions of formic, acetic, propionic, and *n*-butyric acids. As we are concerned with completely miscible systems, we are limited to these four members of the homologous series. The results are closely similar to those of Nestler and Cassidy (*J. Amer. Chem. Soc.*, 1950, **72**, 680).

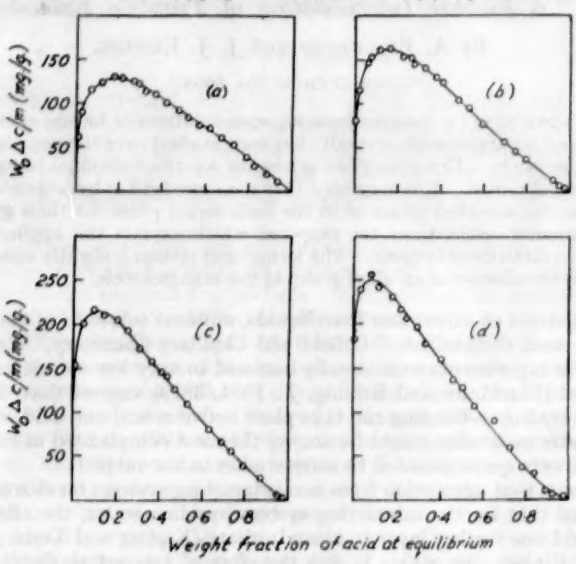
Figs. 2—4 show the adsorption isotherms for the individual components, obtained from vapour-phase experiments. This procedure was originally suggested by Williams (*Medd. K. Vetenskapsakad. Nobelinst.*, 1913, **2**, No. 27), who attempted to apply it to the acetic acid–water system. He found that a long period was required to establish equilibrium and failed to produce complete isotherms because his solutions were attacked by fungus. We have succeeded in applying his method to aqueous solutions of the first three acids, for which increasing times are required to reach equilibrium, but found that the time available was inadequate to reach equilibrium for the fourth.

An analysis of the isotherms of concentration change in terms of Kipling and Tester's monolayer theory for non-interacting systems failed (see Figs. 2—4), as did the simple analysis for the pyridine–water system. Comparison of the three vapour-phase results suggests a possible elaboration. The number of millimoles of water adsorbed per g. of charcoal *decreases* (at corresponding concentrations) as the number of millimoles of acid adsorbed decreases (from formic to propionic acid). The only simple way in which this can occur is for the acid molecules to be adsorbed with their major axes along the solid surface, and not perpendicular to it as has sometimes been assumed for aliphatic substances (*e.g.*, by Lemieux and Morrison, *Canad. J. Res.*, 1947, **25**, *B*, 440) by analogy with close-packed (insoluble) films on aqueous substrates.

The molecules then have the orientations shown in Fig. 6 with respect to the solid surface represented as horizontal. The significance of these is best appreciated by reference to models (cf. Kipling and Norris, *J. Colloid Sci.*, 1953, **8**, 547).

This suggestion is supported by a comparison of the ratios of the molar volumes for the

FIG. 1. *Isotherms of concentration change for adsorption from mixtures of*: (a) *formic acid and water*, (b) *acetic acid and water*, (c) *propionic acid and water*, (d) *butyric acid and water*.



FIGS. 2—5. *Adsorption (individual isotherms) from*:

Fig. 2. *Formic acid–water.* Fig. 3. *Acetic acid–water.*

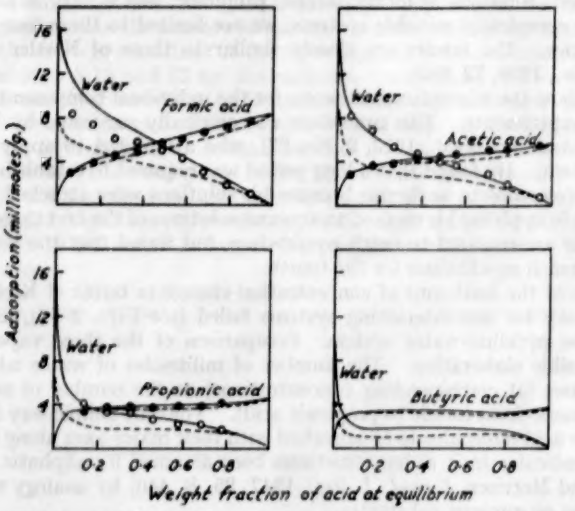


Fig. 4. *Propionic acid–water.* Fig. 5. *Butyric acid–water.*

● Vapour-phase results (acids). ○ Vapour-phase results (water). – – – Calc. from liquid-phase results on the assumption that water is adsorbed as monomer. —— Calc. from liquid phase results on the assumption that water is adsorbed as dimer.

acids in the bulk liquid phase and the molecular areas in the adsorbed monolayers (obtained from experiments with the single vapours). These are shown in the annexed Table. In this, a further comparison is also made with the ratios of the calculated molecular areas of the acids, assumed to be adsorbed with the orientations shown in Fig. 6; the alkyl chains lie along the surface, the planes of carboxyl groups are perpendicular to the surface, and the molecules are assumed to be associated, with consequent shortening of the length of the monomeric unit.

FIG. 6. *Configurations of adsorbed fatty acids.*

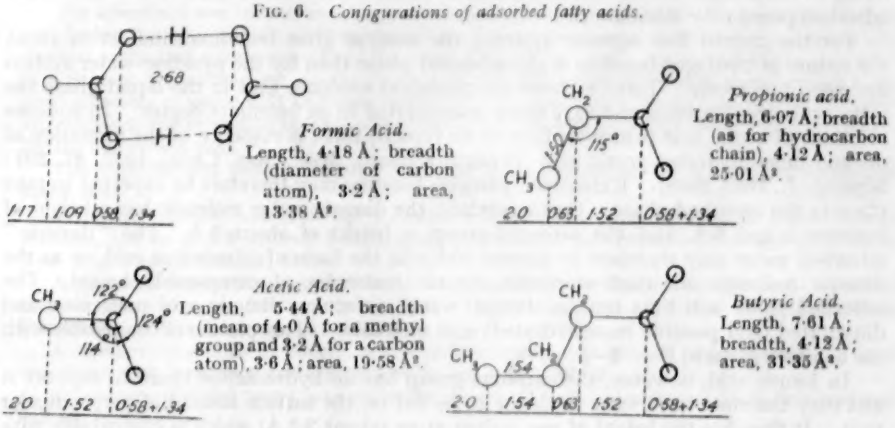
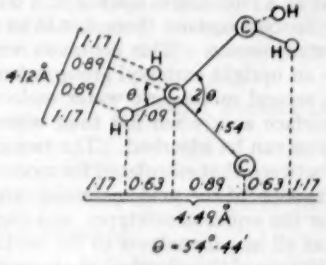

2·68
1·17 1·09 0·58 1·34
Formic Acid.
Length, 4·18 Å; breadth (diameter of carbon atom), 3·2 Å; area, 13·38 Å².
CH3
CH2
1·52
115°
2·0 0·63 1·52 0·58+1·34
Propionic acid.
Length, 6·07 Å; breadth (as for hydrocarbon chain), 4·12 Å; area, 25·01 Å².
CH3
122°
124°
114°
2·0 1·52 0·58+1·34
Acetic Acid.
Length, 5·44 Å; breadth (mean of 4·0 Å for a methyl group and 3·2 Å for a carbon atom), 3·6 Å; area, 19·58 Å².
CH2
CH3
1·54
2·0 1·54 0·63 1·52 0·58+1·34
Butyric Acid.
Length, 7·61 Å; breadth, 4·12 Å; area, 31·35 Å².

FIG. 7. *Dimensions of hydrocarbon chain.*



Acid	Millimoles/g. adsorbed	Ratio of molecular areas (exptl.)	Calc. molecular areas (sq. Å)	Ratio of molecular areas (calc.)	Ratio of molar volumes
Formic	8·42	1	13·38	1	1
Acetic	5·65	1·49	19·58	1·46	1·53
Propionic	4·50	1·87	25·01	1·87	1·96
n-Butyric	3·60	2·34	31·35	2·35	2·44

[The dimensions of the molecules are shown in Fig. 6, and are based on the means of values given by Morrison and Robertson (*J.*, **1949**, 980, 987, 993, 1001) together with the van der Waals radii of 2·0 and 1·17 Å for the methyl group and hydrogen atom, respectively. With this value for the hydrogen atom, the cross-section of the hydrocarbon chain can be represented as a rectangle of sides 4·12 and 4·49 Å (Fig. 7), giving an area of 18·5 sq. Å, which is close to the observed value (Müller, *Proc. Roy. Soc.*, **1927**, *A*, **114**, 542; **1928**, *A*, **120**, 437).]

The close correspondence between the three sets of ratios implies that the increase, from formic to butyric acid, of both molecular area and molar volume is due to increase in one dimension only.

With the orientation shown in Fig. 6, there is little to choose, in analysing the isotherms of concentration change, between assuming that the acids are monomeric and assuming some degree of polymerisation. On the other hand, we have previously assumed, with success, that the water is adsorbed in the dimeric form. Figs. 3 and 4 show that this

assumption allows a satisfactory analysis to be made for the systems acetic acid–water and propionic acid–water. Although we have no direct experimental confirmation of the analysis for the butyric acid–water system, the analysis shown in Fig. 5 seems satisfactory when compared with those of Figs. 3 and 4.

From Fig. 2 it will be seen that for the formic acid–water system the experimental points lie between the curves for the two theoretical analyses. We suggest that this is due to the anomalous behaviour of formic acid, as the first member of the homologous series, owing to the absence of a hydrocarbon chain. A further consideration of the nature of the adsorbed phase may elucidate this.

For the present four aqueous systems, the analysis gives less direct indication about the nature of hydrogen-bonding in the adsorbed phase than for the pyridine–water system discussed previously. There is, however, abundant evidence that in the liquid phase the fatty acids are dimerised and that water is associated to an indefinite degree. In aqueous solutions of acetic acid (which we take to be typical) there is evidence of the formation of di- and mono-hydrated acetic acid (Fénéant-Eymard, *Mém. Serv. Chim.*, 1952, **37**, 297; Kipling, *J.*, 1952, 2858). Extensive hydrogen–bonding may therefore be expected to take place in the adsorbed phase. On the surface, the dimeric water molecule has a height of between 5 and 6 Å, and the carboxyl group a height of about 5 Å. The "dimeric" adsorbed water may therefore be present either in the form of dihydrated acid, or as the dimeric molecule adsorbed alongside organic molecules of comparable height. The adsorbed phase will thus contain dimeric water molecules, dimeric acid molecules, and dihydrated (and possibly monohydrated) acid molecules. This picture is compatible with the analyses given in Figs. 3—5.

In formic acid, however, the carboxyl group has no hydrocarbon chain to support it and may therefore have some tendency to lie flat on the surface instead of perpendicular to it. It then has the height of one carbon atom (about 3·2 Å) which is comparable with the height of a monomeric instead of a dimeric water molecule. Thus in the *second* layer from the charcoal surface, there should be more opportunity for direct competition between the two components. (This contrasts with the position of a monomeric water molecule alongside an upright carboxyl group, where, in general, space is only available for adsorption of a second monomeric water molecule.) Moreover, the carboxyl group occupies a greater surface area when flat than when vertical, and this again reduces the extent to which water can be adsorbed. The two effects combine to give adsorption of water intermediate between that calculated for monomeric water only and that for dimeric water only. Only a fraction of the acid molecules would have to lie flat to account for the observed results for the aqueous mixtures, and there is no need to suppose that this orientation is adopted at all in a monolayer of the acid alone.

This picture of the adsorbed phase provides an interpretation of Traube's rule as applied to these systems (Freundlich, *op. cit.*). The "horizontal" orientation of the acid molecules means that, when equal numbers of molecules of formic, acetic, propionic, and butyric acids are adsorbed, the number of water molecules which can be adsorbed on the remainder of the surface decreases in this order. Further, the increasing heat of adsorption per molecule to be expected as the number of methylene groups in the hydrocarbon chain increases would lead one to expect that the higher acids would compete with water for the hydrophobic surface more effectively than the lower acids. These two effects, operating in the same direction, combine to give the result expressed in Fig. 1. The explanation is similar to that given by Langmuir (*J. Amer. Chem. Soc.*, 1917, **39**, 1848) for the adsorption of the lower fatty acids at the air–water interface of dilute aqueous solutions, though this has been criticised by Ward (*Trans. Faraday Soc.*, 1946, **42**, 399) on the grounds that the acid molecules are more likely to be spheroidal than cylindrical. It is difficult to see how molecules as small as those of formic and acetic acids can be regarded as spheroidal, and the concept can be applied only qualitatively to butyric acid, however well it may apply to higher acids. On the other hand, the concept of a linear orientation does allow an approximate calculation to be made of the molecular areas, the results being shown in the Table above. Jones and Saunders (*J.*, 1951, 2944) concluded that, at the nitromethane–air interface, fatty acid molecules arrange themselves intermediately between a horizontal and

a random orientation. They point out that in this sytem the surface forces are inadequate to produce a completely ordered surface layer. Stronger forces might be expected to operate at a charcoal surface. It may be added that, in a different approach to this manifestation of Traube's rule, Hansen and Craig (*J. Phys. Chem.*, 1954, **58**, 211) found a regularity in behaviour for acetic, propionic, and butyric acids, but unfortunately they did not study formic acid.

Experimental

The absorbent was the steam-activated coconut-shell charcoal described previously (Kipling and Tester, *loc. cit.*). Acetic acid reacts with the ash in the charcoal, even that which is left after Soxhlet extraction with water (Blackburn and Kipling, *loc. cit.*). It was therefore extracted in a Soxhlet apparatus with glacial acetic acid and subsequently washed with distilled water until all traces of acetic acid had been removed. The resulting charcoal caused only negligible alterations to the refractive indexes of the four acids, when shaken with them in the ratios used for the adsorption runs.

The experimental procedures have been described previously, as has the purification of acetic acid.

"AnalaR" formic acid (98—100%), twice distilled from phosphoric oxide under reduced pressure, had m. p. 8·3° and n_D^{20} 1·3713, in agreement with the values of Dreisbach and Martin (*Ind. Eng. Chem.*, 1949, **41**, 2875).

A commercial sample of propionic acid was fractionally distilled, refractionated from dried alumina gel, and again fractionally distilled. The product had n_D^{20} 1·3858, as compared with Dreisbach and Martin's value of 1·3865.

A commercial sample of butyric acid was fractionally distilled; it had n_D^{20} 1·3980, in good agreement with Dreisbach and Martin's value (cf. Jones and Saunders, *loc. cit.*).

Laboratory distilled water was redistilled in an all-glass apparatus and the fraction used had n_D^{20} 1·3330.

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The University, Hull. [*Received, November 23rd*, 1954.]

Cyanamides. Part VIII. The Interaction of 1-Arylbiurets and Arenesulphonyl Chlorides.*

By Frederick Kurzer and J. Roy Powell

[Reprint Order No. 6001]

The interaction of 1-arylbiurets or *N*-aryl-*N'*-cyanoureas with arenesulphonyl chlorides in pyridine produces aryl *iso*cyanates and triarenesulphonylmelamines as main products. The mechanism of these reactions is discussed.

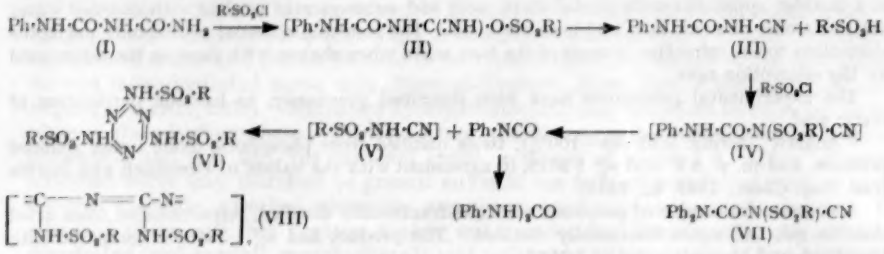
Unlike acylureas and their thio-analogues, sulphonylureas and sulphonylthioureas are not obtainable by the direct action of the appropriate acid chlorides upon ureas (Kurzer, *Chem. Reviews*, 1952, **50**, 1, 13). Aromatic ureas and thioureas react with arenesulphonyl chlorides, with elimination of the elements of water or hydrogen sulphide, to yield *N*-arenesulphonyl-*N*-arylcyanamides (Part III, *J.*, 1949, 1034, 3029; Part IV, 1950, 3269). *iso*-Ureas and *iso*thioureas, on the other hand, readily form *N*-sulphonyl derivatives by a modified Hinsberg procedure. The present paper reports analogous reactions of biurets; in their essentials, the results may be correlated satisfactorily with those in the urea series.

The reaction between 1-arylbiurets and arenesulphonyl chlorides in pyridine, under

* Part VII, *J.*, 1954, 4152. Most of the present work has been summarised in *Chem. and Ind.*, 1953, 195.

the usual experimental conditions (Part II, *loc. cit.*), afforded *iso*cyanates and trisulphonylmelamines (VI) as main products. 1-Phenylbiuret and toluene-*p*-sulphonyl chloride, for example, gave *s*-diphenylurea (from the primary product, phenyl *iso*cyanate) and tri(toluene-*p*-sulphonyl)melamine in 60 and 45% yield, respectively. The comparatively low yields of the latter were due to the formation of by-products in a parallel reaction (see below).

The main reaction is accounted for by a mechanism, outlined in the annexed scheme (I—VI), which is closely related to those that have proved satisfactory for the corresponding reactions of aromatic ureas (Part III, *J.*, 1949, 3033) and thioureas (Part IV, *loc. cit.*). In this sequence, the first stage of the interaction is the formation of unstable 1-aryl-4-



O-sulphonyl-4-*iso*biurets (II). In common with other imidosulphonate structures incorporating the ·C(O·SO_2R):NH grouping (Oxley, Partridge, Peak, and Short, *J.*, 1948, 1514, 1618; Kurzer, *Chem. Reviews*, *loc. cit.*), these decompose instantly with elimination of arenesulphonic acids to yield the corresponding cyano-derivative, in this instance *N*-aryl-*N'*-cyanoureas (III). Further interaction of these intermediates with excess of sulphonyl halide affords *N*-aryl-*N'*-cyano-*N'*-sulphonylureas (IV). Observations on the interaction of *N*-cyano-*N'*-sulphonylguanidines and sulphonyl chlorides (Part VI, *J.*, 1953, 2531), and the present results, suggest that structures incorporating a ·N(SO_2R)·CN grouping in proximity to a mobile hydrogen atom are labile, and decompose with elimination of the elements of sulphonylcyanamides. Thus, the postulated intermediate sulphonylcyanoureas (IV) break down into aryl *iso*cyanates and arenesulphonylcyanamides (V), the latter polymerising to trisulphonylmelamines (VI) and other polymeric products (see below). The fact that cyanosulphonylureas (IV) are split spontaneously *during* the reaction, and not by hydrolytic reagents used in the subsequent isolation process (cf. Experimental section), was confirmed by the addition of suitable reaction mixtures to anhydrous light petroleum, aryl *iso*cyanate being then isolated. The formulation of cyanosulphonylureas, as (IV), in preference to alternative *O*-sulphonyl*iso*urea structures [Ph·N:C(O·SO_2·R)·NH·CN and tautomeric forms] is regarded as justified in view of the acidic character of the hydrogen atom of the cyanamide grouping in cyanoureas (III).

The correctness of the suggested mechanism presupposed that *N*-aryl-*N'*-cyanoureas and 1-arylbiurets should form the same products with sulphonyl halides. This requirement was fulfilled, cyanoureas (III) reacting generally more smoothly to give better yields, probably because the two initial stages of the reaction sequence (I—VI) are eliminated. *N*-Cyano-*N'*-phenylurea and toluene-*p*-sulphonyl chloride in pyridine at 80°, for example, produced *s*-diphenylurea and tri(toluene-*p*-sulphonyl)melamine in 65% and 58% yields, respectively.

The last stage of the suggested mechanism [*i.e.*, (V ⟶ VI)] has not been confirmed experimentally because benzene- and toluene-*p*-sulphonylcyanamide were not obtainable except in the form of their metallic salts. In contrast, free aroylcyanamides can be isolated without difficulty (*e.g.*, benzoylcyanamide: Hantzsch and Dollfus, *Ber.*, 1902, **35**, 255; Diels and Wagner, *Ber.*, 1912, **45**, 876; Crowther, Curd, and Rose, *J.*, 1948, 586). Arenesulphonylcyanamide salts have been described by Hebenstreit (*J. prakt. Chem.*, 1890, **41**, 97), who claimed their conversion, by mineral acids, into free sulphonylcyanamides. In the present work, Hebenstreit's experimental observations were confirmed, and the identity

of the salts established by their conversion into sulphonylthioureas with hydrogen sulphide in pyridine–triethylamine by the method of Fairfull, Low, and Peak (*J.*, 1952, 742). All attempts to isolate the free acids from the sulphonylcyanamide salts, however, under Hebenstreit's or other conditions, gave arenesulphonylureas, or resulted, on more drastic treatment, in partial hydrolysis to arenesulphonamides. Excepting the single representative of the alkyl series described, Hebenstreit's alleged sulphonylcyanamides contained, on the basis of their composition " a molecule of water of crystallisation " which was not given off below their decomposition points; their reported stability towards acids, and their thermal decomposition into sulphonamide and cyanuric acid (recently shown to be a reaction of sulphonylureas; cf. Part V, *J.*, 1951, 1258) show plainly that Hebenstreit's aromatic products were arenesulphonylureas. Brief treatment of sodium or calcium sulphonylcyanamides with boiling mineral acid has in fact been used for the preparation of *p*-acetamido- (Winnek, Anderson, Marson, Faith, and Roblin, *J. Amer. Chem. Soc.*, 1942, **64**, 1682) and *p*-nitrobenzenesulphonyl-urea (Backer and Moed, *Rec. Trav. chim.*, 1947, **66**, 335).

The remarks concerning stage (IV ⟶ V) imply that fully substituted sulphonylcyanoureas, which lack mobile hydrogen atoms, should not decompose spontaneously. This expectation was realised by the preparation of a sulphonyl derivative of *N*-cyano-*N'N'*-diphenylurea, formulated as (VII). The required cyanourea was readily obtained from diphenylcarbamoyl chloride (reaction 1); it was remarkably resistant to the action of alkalis, but was rapidly hydrolysed to diphenylamine by boiling hydrochloric acid; brief treatment with concentrated sulphuric acid at 25° gave fair yields of 1 : 1-diphenylbiuret (reaction 2). Reactions (1) and (2) are a useful extension of one of the classical biuret syntheses (Baumann *Ber.*, 1875, **8**, 708; Hecht, *Ber.*, 1892, **25**, 749) to 1 : 1-disubstituted biurets. In this connexion, mention may be made of Biltz and Jeltsch's unsuccessful efforts (*Ber.*, 1923, **56**, 1914) to prepare analogous substituted biurets by condensing dimethylcarbamoyl chloride with urea and its homologues; the present method appears to by-pass these difficulties.

$$Ph_2N{\cdot}COCl + NH_2{\cdot}CN \longrightarrow Ph_2N{\cdot}CO{\cdot}NH{\cdot}CN + HCl \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$Ph_2N{\cdot}CO{\cdot}NH{\cdot}CN + H_2O \longrightarrow Ph_2N{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NH_2 \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Both the above reactions (I ⟶ VI, and III ⟶ VI), but more particularly the biuret–arenesulphonyl chloride interaction, gave also varying quantities (20—40%) of non-homogeneous by-products, the composition of which approximated to that of arenesulphonylcyanamides. These products were highly soluble non-crystalline acidic solids of high molecular weight; they were partially fractionated and purified by repeated reprecipitation from their alkaline or alcoholic solution (cf. Experimental section). Hydrolysis, by concentrated sulphuric acid or ethanolic hydrogen chloride (cf. Part VI, *loc. cit.*), afforded the appropriate sulphonic acid or sulphonamide, respectively, thus confirming the presence of arenesulphonamido-residues in their structures.

Analogous products resulted in moderate yields from the interaction of cyanamide and arenesulphonyl chlorides in pyridine. The mode of formation, the ultimate composition, and the non-homogeneous nature of these substances suggest their provisional formulation as polymers (other than melamines) of arenesulphonylcyanamides. While no definite structure can be advanced at this stage, the possible existence of linear polymers (VIII) of varying chain length, analogous in structure with Sidgwick's suggested formula for cyamelide (Taylor and Baker, " Sidgwick's Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1937, p. 323), may be borne in mind.

In contrast to *iso*urea ethers, which yield *N*-sulphonyl derivatives readily (Cox and Raymond, *J. Amer. Chem. Soc.*, 1941, **63**, 300; 1942, **64**, 2225), the structurally related 4-methyl-1-phenyl-4-*iso*biuret failed to react with sulphonyl chlorides in alkaline media. In pyridine, small quantities (3—8%) of triarenesulphonylmelamine were produced, probably by previous demethylation of the *iso*biuret by the pyridinium chloride formed *in situ* (cf. Kurzer, *J.*, 1953, 3360), followed by the usual reaction (I—VI).

Attention may be drawn to the powerfully sweet taste, previously unrecorded, of *N*-cyano-*N'*-phenylurea. The introduction of the cyano-group into phenylurea, known to

possess a strong bitter taste, thus causes a remarkable reversal of this physiological property. *N*-Cyano-*N'*-α-naphthylurea was tasteless.

Experimental

The pyridine used was the commercially available anhydrous grade. The identity of triarenesulphonylmelamines was confirmed in all cases by mixed m. p. determinations with authentic samples prepared from cyanuric chloride (Part VII, *loc. cit.*), and from *N*-arenesulphonyl-*N'*-cyanoguanidines (Part VI, *loc. cit.*).

1-Phenylbiuret was prepared by McKee's method (*Amer. Chem. J.*, 1901, **26**, 253) in 62—70% yield from 4-methyl-1-phenyl-4-*iso*biuret. After four crystallisations from absolute ethanol it formed compact prisms, m. p. 170—171° (decomp.) (inserted at 145°; temp. raised at 4° per min.). The m. p. of the product depends on the rate of heating, and has variously been given between 156° and 167° (McKee, *loc. cit.*; Blair, *J. Amer. Chem. Soc.*, 1934, **56**, 904).

4-*Methyl*-1-α-*naphthyl*-4-iso*biuret*.—A solution of methyl*iso*urea hydrochloride (Kurzer and Lawson, *Org. Synth.*, 1954, **34**, 67) (12·2 g., 0·11 mole), in water (15 ml.), rendered alkaline with aqueous potassium hydroxide (27 ml., 25% w/v., 0·12 mole) was slowly treated with α-naphthyl *iso*cyanate (16·9 g., 0·1 mole), with good shaking during 10 min. at <25° (cooling); agitation was then continued for 0·5 hr. The granular solid was collected, air-dried, and extracted with boiling ethanol (4 × 50 ml.). The ethanol-insoluble residue was di-α-naphthylurea, m. p. 286—287° (2·3 g.). The alcoholic extracts deposited, on cooling and partial evaporation, white crystals (m. p. 140—145°; total 13·6 g., 56%) which gave, on crystallisation from ethanol (20 ml. per g.), lustrous platelets of 4-*methyl*-1-α-*naphthyl*-4-iso*biuret*, m. p. 141—142° (decomp.) (Found: C, 64·4; H, 5·4; N, 16·8. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·35; N, 17·3%).

1-α-*Naphthylbiuret*.—A suspension of 4-methyl-1-α-naphthyl-4-*iso*biuret (12·15 g., 0·05 mole) in hydrochloric acid (3N, 180 ml.; contained in a large flask; subsequent severe frothing) was slowly heated under reflux until brisk effervescence indicated the beginning of the interaction; the source of heat was then temporarily withdrawn. The reaction was completed by gentle boiling until no more methyl chloride was evolved (15—20 min.). The suspension was cooled to 0°, and the granular solid [m. p. 220—224° (decomp.); 10—10·5 g.] collected, dried, and crystallised from ethanol (150 ml. per g.), white feathery needles of 1-α-naphthylbiuret, m. p. 214—215° (decomp.), being obtained (8·6—9·15 g., 75—80%) (Found: N, 18·6. Calc. for $C_{12}H_{11}O_2N_3$: N, 18·3%).

Interaction of 1-*Phenylbiuret and Toluene*-p-*sulphonyl Chloride*.—A solution of 1-phenylbiuret (3·58 g., 0·02 mole) in pyridine (30 ml.) was treated with toluene-*p*-sulphonyl chloride (11·44 g., 0·06 mole) at 20°. The orange-red liquid (the temperature of which did not rise spontaneously) was kept at 85—90° during 20 min., stirred into ice (250 g.), and acidified to Congo-red with concentrated hydrochloric acid (35 ml.). During several hours' storage, the upper oily orange-brown layer (which smelled powerfully of phenyl *iso*cyanate) solidfied gradually, with simultaneous slow effervescence, to a brittle sponge-like mass. The powdered product was extracted with aqueous sodium hydroxide (12%; 40, 30, and 20 ml.; at 20°, 30°, and 40° respectively). The collected undissolved product (m. p. 215—225°; 1·10—1·30 g., 52—61%) was *s*-diphenylurea, forming needles, m. p. and mixed m. p. 236—238°, from ethanol. Acidification of the alkaline filtrate to Congo-red with concentrated hydrochloric acid gave a white solid; the collected air-dried powder (3·8 g.) was added to boiling ethanol (50 ml.): the red solution rapidly deposited lustrous crystals on cooling. [A second crop was obtainable by evaporating the ethanol filtrates to dryness, redissolving the residual oil in 12% alkali, and adding the product precipitated by acid to a fresh portion of boiling ethanol (ethanolic filtrates therefrom: A).] The collected crystalline solid (m. p. 278—282°; 1·57—1·75 g., 40—45%) gave, on crystallisation from ethanol, platelets of tri(toluene-*p*-sulphonyl)melamine, m. p. 282—284° (Found: C, 49·2; H, 4·6; N, 13·9; S, 15·9. Calc. for $C_{24}H_{24}O_6N_6S_3$: C, 49·0; H, 4·1; N, 14·3; S, 16·3%).

The ethanolic filtrates A, from which no more trisulphonylmelamine separated, contained varying quantities of an oil, highly soluble in organic solvents and alkalis, which was isolated by precipitation from its alkaline solution by mineral acid, as a white to pink powder, of indefinite m. p. The results of analysis and mol. wt. determinations suggest the presence of a higher polymeric form of toluene-*p*-sulphonylcyanamide (yield, 1·2—1·7 g.; 30—43%, calc. as polymeric sulphonylcyanamide) (cf. last paragraph, Experimental).

1-Phenylbiuret was recovered almost quantitatively after treatment with toluene-*p*-sulphonyl chloride in acetone–aqueous alkali (experimental details as in Part VI, *J.*, 1953, 2533).

Cognate Experiments.—The interaction of 1-phenylbiuret and benzenesulphonyl chloride

under the above conditions gave *s*-diphenylurea (68%), ethanol-solvated tribenzenesulphonylmelamine, m. p. 150—152° (decomp.) (38%) (Found: C, 47·0; H, 4·1; N, 14·7. Calc. for $C_{21}H_{18}O_6N_6S_3,C_2H_6O$: C, 46·6; H, 4·05; N, 14·2%), and low-melting (60—70°) acidic material (45%, calc. as polymeric benzenesulphonylcyanamide).

1-Phenylbiuret and toluene-*o*-sulphonyl chloride similarly gave *s*-diphenylurea (62%), tri(toluene-*o*-sulphonyl)melamine, m. p. 292—294° (16%), and low-melting acidic material (45%).

1-α-Naphthylbiuret (2·30 g., 0·01 mole), suspended in pyridine (20 ml.), was treated at 80° with toluene-*p*-sulphonyl chloride (7·6 g., 0·04 mole) during 5 min., and the resulting deep-red liquid kept at 95° during 30 min., and worked up as above. It afforded *s*-di-α-naphthylurea, m. p. 286—287° (decomp.) (82%), tri(toluene-*p*-sulphonyl)melamine, m. p. 282—284° (45%), and low-melting acidic material (35%). Under the less vigorous standard conditions (see above), much unchanged 1-α-naphthylbiuret, m. p. and mixed m. p. 223—225° (up to 40%), was recovered from the alkali-insoluble product and was separated from the *s*-di-α-naphthylurea by its solubility in ethanol.

4-Methyl-1-phenyl-4-*iso*biuret, treated with arenesulphonyl chloride in pyridine, gave 3—8% of triarenesulphonylmelamine (presumably by preliminary demethylation of the *iso*-biuret by pyridinium chloride). It failed to react with arenesulphonyl chloride in aqueous or aqueous acetone media in the presence of alkali.

N-*Cyano*-N′-*α-naphthylurea*.—A solution of cyanamide (6·3 g., 0·15 mole) (*Org. Synth.*, 1954, **34**, 67) in water (25 ml.), made alkaline with sodium hydroxide (12% w/v., 36 ml.; 0·11 mole) was treated, with good shaking, at 20—25° (slight external cooling required) with α-naphthyl *iso*cyanate (18·6 g., 0·11 mole) during 30 min. A trace of separated di-α-naphthylurea was filtered off, and the clear filtrate *just* acidified to Congo-red with concentrated hydrochloric acid (dropwise). The crystalline precipitate was collected at 0°, washed with ice-water (5 × 20 ml.), and dried in a vacuum over phosphoric oxide. The crude product [m. p. 142—145° (decomp., resolidifying at once); 19·7 g., 85%] gave, after two crystallisations from acetone–light petroleum (12 and 6 ml., respectively, per g.; recovery 60% per crystallisation), lustrous prisms of N-*cyano*-N′-*α-naphthylurea*, m. p. 148—149° (decomp.) (Found: N, 19·7. $C_{12}H_9ON_3$ requires N, 19·9%).

Interaction of N-*Cyano*-N′-*phenylurea and Toluene*-p-*sulphonyl Chloride*.—(*a*) *N*-Cyano-*N*′-phenylurea (3·22 g., 0·02 mole), dissolved in pyridine (15 ml.), was treated with toluene-*p*-sulphonyl chloride (7·62 g., 0·04 mole) at room temperature, and the solution kept at 80° during 20 min. The deep-red liquid was added to ice (150 g.), and the whole acidified to Congo-red with concentrated hydrochloric acid (20 ml.). The observations, and the method of isolating the products, were as described for the corresponding reaction of 1-phenylbiuret (see above). In this way, the following were obtained: *s*-diphenylurea (1·38 g., 65%), m. p. and mixed m. p. 236—238°; tri(toluene-*p*-sulphonyl)melamine (2·27 g., 58%), m. p. 282—284°; and low-melting (65—75°) acidic material (1·18 g., 30%, calc. as polymeric toluene-*p*-sulphonylcyanamide).

(*b*) The deep-red reaction mixture obtained as in (*a*) was stirred with anhydrous light petroleum (b. p. 60—80°; 3 × 60 ml.), and the extracts were decanted (combined extracts: A). The residual oil solidified slowly in contact with water (10 ml.); it was separated, as usual, by sodium hydroxide, into *s*-diphenylurea (0·4 g., 19%), and tri(toluene-*p*-sulphonyl)melamine (52%), m. p. 282—284°. Evaporation of the petroleum extracts A gave an oil which smelled powerfully of phenyl *iso*cyanate: addition of aniline (3·7 g., 0·04 mole), followed by heating at 90° during 0·5 hr., gave a product which was extracted with aqueous sodium hydroxide (6%; 3 × 15 ml.). The insoluble residue was *s*-diphenylurea (2·85 g., 67%); acidification of the filtrate precipitated toluene-*p*-sulphonanilide (0·85 g.), m. p. and mixed m. p. 100—102° (from benzene–light petroleum) (Found: C, 63·1; H, 5·3; N, 5·4. Calc. for $C_{13}H_{13}O_2NS$: C, 63·2; H, 5·3; N, 5·7%). The last-mentioned product arose probably from the excess of toluene-*p*-sulphonyl chloride, dissolved by the light petroleum, and the added aniline.

N-Cyano-*N*′-phenylurea was recovered unchanged after treatment with toluene-*p*-sulphonyl chloride in acetone–aqueous alkali (experimental details as in Part VI).

Cognate Experiments.—The reaction of *N*-cyano-*N*′-phenylurea and toluene-*o*-sulphonyl chloride (procedure *a*) gave *s*-diphenylurea (65%), and tri(toluene-*o*-sulphonyl)melamine (36%), m. p. 293—294°. Interaction of *N*-cyano-*N*′-α-naphthylurea (0·01 mole) and toluene-*p*-sulphonyl chloride (0·04 mole) at 95° during 30 min., followed by isolation according to procedure (*a*), afforded *s*-di-α-naphthylurea (54%), m. p. and mixed m. p. 285—287° (decomp.), and tri(toluene-*p*-sulphonyl)melamine (38%), m. p. 282—284°.

N-Cyano-N′N′-diphenylurea.—To cyanamide (10·1 g., 0·24 mole; *Org. Synth.*, 1954, **34**, 67) in water (40 ml.), previously filtered with carbon, aqueous sodium hydroxide (25 ml., 20% w/v, 0·125 mole) and acetone (50 ml.) were added. This stirred solution was treated, at room temperature, with a solution of diphenylcarbamoyl chloride (13·9 g., 0·06 mole) in acetone (30 ml.) during 2—2½ hr., a further portion of aqueous sodium hydroxide (0·125 mole) being gradually added during the second half of the addition to keep the liquid strongly alkaline to litmus. Stirring was then continued for 1—1½ hr., and more acetone added if necessary, to redissolve any solid which tended to separate. Air was now drawn over the surface of the stirred solution to remove most of the acetone, and the residual liquid (L) diluted with water (100 ml.). A small quantity of separated solid (consisting of unchanged diphenylcarbamoyl chloride, m. p. 86°) was filtered off, and the clear filtrate acidified at 0° with concentrated hydrochloric acid. The precipitated crystalline solid was collected, washed with water, and then with ether (3 × 20 ml.; ethereal washing liquid: A) and air-dried (m. p. 138—144°, after sintering at 130°; 12·1—12·8 g.). Two crystallisations from acetone–light petroleum (10 and 4 ml., respectively, per g.) gave lustrous plates of *N-cyano-N′N′-diphenylurea*, m. p. 153—154° (Found: C, 70·35; H, 4·3; N, 17·4. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·7%) (yield, including material from the mother-liquors, 9·25—12·1 g., 65—85%). The ethereal washing liquid A deposited diphenylamine (1·0 g., 10%), m. p. and mixed m. p. 52—54°, on evaporation.

Alternatively, the filtered liquid L, without previous dilution, was set aside at 0° during 48 hr. The separated crystalline solid (m. p. 88—90°; 14—14·8 g., 90—95%) was collected and recrystallised from acetone (5 ml. per g., recovery 80%) and lustrous needles of the *sodium derivative*, m. p. 89—91°, were obtained. Its identity was established by reconversion into *N*-cyano-*N′N′*-diphenylurea (carried out by acidification of its aqueous solution).

N-Cyano-*N′N′*-diphenylurea was recovered almost quantitatively (*a*) after being refluxed with aqueous 1·5N-sodium hydroxide during 1 hr, or (*b*) after treatment with excess of 6% hydrogen peroxide in 1·5N-sodium hydroxide at 50—60° during 3 hr. Brief refluxing with N-hydrochloric acid caused quantitative hydrolysis to diphenylamine.

1 : 1-*Diphenylbiuret.*—Finely powdered *N*-cyano-*N′N′*-diphenylurea (2·37 g., 0·01 mole) was stirred within 4—5 min. into concentrated sulphuric acid (12 ml.) at 25—30° (cooling). Complete dissolution occurred during the next 2—3 min., and stirring at 25° was continued for a total of 15 min. The almost colourless liquid was treated with crushed ice (30 g.) in one portion. The resulting white precipitate was collected immediately, washed with water, and dried in a desiccator over phosphoric oxide. The white solid (2·2 g.) was dissolved in acetone (120 ml.) –ethanol (10 ml.), and the solution filtered with suction, evaporated to small volume (20 ml.) under reduced pressure, and set aside. It deposited a white semicrystalline solid (1·4 g.) which consisted, after two crystallisations from ethanol (30 ml. per g.), of minute prisms of 1 : 1-*diphenylbiuret*, m. p. 175—178° (decomp.) (1·12 g., 44%), soluble in aqueous alkalis, and re-precipitated by acids. Repeated crystallisation from ethanol raised the m. p. to 182—183° (decomp.; somewhat subject to the rate of heating) (Found: C, 66·2; H, 5·1; N, 16·5. $C_{14}H_{13}O_2N_3$ requires C, 65·9; H, 5·1; N, 16·5%).

N-Cyano-N-m-nitrobenzenesulphonyl-N′N′-diphenylurea.—A solution of *N*-cyano-*N′N′*-diphenylurea (2·37 g., 0·01 mole) in pyridine (20 ml.) at room temperature was treated with *m*-nitrobenzenesulphonyl chloride (3·32 g., 0·015 mole) with cooling. After being kept at 15° during 1 hr., the liquid was added to ice (100 g.) and concentrated hydrochloric acid (20 ml.). The collected dried pale-pink solid (4·15 g.) was dissolved in a boiling mixture of ethanol (25 ml.) and acetone (10 ml.); the clear (filtered) liquid deposited, on prolonged storage, a white granular solid (1·7—2·2 g., 40—52%), which gave, on crystallisation from benzene–light petroleum, needles of *N-cyano-N-m-nitrobenzenesulphonyl-N′N′-diphenylurea*, m. p. 200—202° (decomp.) (Found: C, 56·4; H, 3·7; N, 13·6; S, 7·2. $C_{20}H_{14}O_5N_4S$ requires C, 56·9; H, 3·3; N, 13·3; S, 7·6%).

Hydrolysis. The above product (1·06 g., 0·0025 mole), suspended in absolute ethanol (120 ml.), was refluxed with passage of anhydrous hydrogen chloride during 10 hr. The resulting clear solution was evaporated nearly to dryness in a vacuum; the residue was made alkaline and stirred with sodium hydroxide (12% w/v; 6 ml.); the undissolved solid was filtered off at 0°, and rinsed with a few drops of water (filtrate A); crystallisation from light petroleum (b. p. 60—80°) gave diphenylamine, m. p. and mixed m. p. 52—53° (total, 0·36 g., 86%). Acidification of filtrate A precipitated *m*-nitrobenzenesulphonamide, which was collected at 0° (0·28 g., 56%) and gave needles, m. p. and mixed m. p. 159—161° (from water).

Toluene-p-sulphonylurea.—A solution of sodium toluene-*p*-sulphonylcyanamide (4·4 g., 0·02 mole) [Hebenstreit, *J. prakt. Chem.*, 1890, **41**, 97; the salt crystallises from a large volume of

acetone–ether in platelets, m. p. 290—294° (decomp.)] in water (20 ml.) and concentrated hydrochloric acid (8 ml.) was boiled for 2 min. The white granular solid (1·93 g., 45%; m. p. 183—184°), which was deposited on cooling, was collected (filtrate A) and crystallised from water and then from acetone–light petroleum (25 and 5 ml., per g., respectively), giving toluene-*p*-sulphonylurea, m. p. 191—192° (decomp., subject to the rate of heating; the m. p. was erroneously given as 200—202° in Part V, *J.*, 1951, 1258) (Found: C, 45·0; H, 4·5; N, 13·4. Calc. for $C_8H_{10}O_3N_2S$: C, 44·9; H, 4·7; N, 13·1%). The aqueous filtrate A gave varying quantities of toluene-*p*-sulphonamide, m. p. and mixed m. p. 136—137°, on evaporation.

Similar results were obtained by storing acidified solutions of sodium toluene-*p*-sulphonylcyanamide at room temperature for 48—72 hr. The salt (1 g.), when refluxed in concentrated hydrochloric acid (30 ml.) during 30 min., was converted nearly quantitatively into toluene-*p*-sulphonamide.

Benzenesulphonylurea.—Sodium benzenesulphonylcyanamide (2·04 g., 0·01 mole), when dissolved in an equivalent of 0·1N-sulphuric acid and evaporated to small volume during 3 hr., gave white cubes of benzenesulphonylurea, m. p. and mixed m. p. 170—171° [cf. Haak, U.S.P. 2,385,571; Hebenstreit, *loc. cit.*, reported m. p. 158° (decomp.)]. A second crop resulted from further evaporation and recrystallisation from aqueous ethanol (total yield: 0·65 g., 33%). The final fractions consisted of a mixture of benzenesulphonylurea and benzenesulphonamide.

*Toluene-*p*-sulphonylthiourea.*—A solution of ammonia (0·68 g., 0·04 mole) in anhydrous *n*-butanol (20 ml.) was saturated with hydrogen sulphide at 0°. Sodium toluene-*p*-sulphonylcyanamide (4·35 g., 0·02 mole) (Hebenstreit, *loc. cit.*) was added, and the suspension heated in a closed vessel at 100° for 6 hr. The crystalline product was filtered off at 0°, washed with *n*-butanol, dried, and dissolved in water (30 ml.). The turbid liquid was filtered with carbon and acidified; the resulting yellow oil was dissolved in ethanol (2 ml., 90%), crystalline plates (0·90 g., 20%) of *toluene-*p*-sulphonylthiourea*, m. p. 128—129° (from ethanol), being slowly deposited (Found: C, 41·8; H, 4·6. $C_8H_{10}O_2N_2S_2$ requires C, 41·7; H, 4·35%). Treatment of a solution of the above sodium salt in pyridine (40 ml.)–triethylamine (2·8 ml.) at 60° for 3 hr. failed to yield the required product. The correctness of the structure of this compound was confirmed by the analogous preparation (in 30% yield) of benzenesulphonylthiourea, m. p. and mixed m. p. (B.P. 595,771; U.S.P. 2,498,782) 137—139° (from ethanol).

*Interaction of Cyanamide and Toluene-*p*-sulphonyl Chloride.*—Cyanamide (4·2 g., 0·1 mole; *Org. Synth.*, 1954, **34**, 67) in pyridine (30 ml.) was treated with toluene-*p*-sulphonyl chloride (21 g., 0·11 mole) during 5 min., and the hot deep-red liquid kept at 80—90° during 15 min. and added to N-hydrochloric acid (300 ml.) at 0°. The air-dried granular buff precipitate (6—9 g.) was dissolved in boiling ethanol (30—50 ml.) and set aside overnight, and the clear liquid (solution A) decanted from a dark viscid deposit. This, on re-dissolution in boiling ethanol, prolonged treatment with carbon, and filtration, gave a solution which deposited small quantities (up to 0·6 g., 3%) of tri(toluene-*p*-sulphonyl)melamine, m. p. 281—283°, in some, but not all, experiments. Addition of solution A to water (300 ml.) containing sodium chloride (2 g.) gave a granular precipitate (5·5—8 g., 28—41% calc. as polymeric toluene-*p*-sulphonylcyanamide), which formed, after two further reprecipitations from alkaline solution, a nearly white amorphous powder, decomposing variously between 70° and 90°. One hour's drying at 80° in a vacuum raised the decomposition range to 135—145° (after sintering at 120—130°). The *substance* was highly soluble in the usual organic solvents except light petroleum (Found: C, 47·9, 48·5; H, 4·3, 4·6; N, 14·7, 14·2; S, 15·0, 15·7. $[C_8H_9O_2N_2S]_n$ requires C, 49·0; H, 4·1; N, 14·3; S, 16·3%). The product did not significantly depress the f. p. of naphthalene or thymol.

Addition of excess of 6N-aqueous potassium hydroxide to an ethanolic solution of the product gave its *potassium salt*, forming lustrous plates when recrystallised from 66% ethanol (Found: C, 40·3; H, 3·25. $[C_8H_7O_2N_2SK]_n$ requires C, 41·0; H, 3·0%). Addition of excess of silver nitrate to an aqueous ammoniacal solution of the product gave the *silver salt* as a white precipitate {Found (volumetrically): Ag, 32·5, 31·9. $[C_8H_7O_2N_2SAg,H_2O]_n$ requires Ag, 33·6%}.

The material was recovered substantially unchanged after being refluxed with acetic acid–acetic anhydride (2 : 3) during 30 min. It did not add the elements of hydrogen sulphide when treated with this gas in ammoniacal butanol under pressure (conditions: cf. Kurzer, *J. Appl. Chem.*, 1951, **1**, 84) or in pyridine–triethylamine (cf. Fairfull, Low, and Peak, *J.*, 1952, 742). It resisted hydrolysis on 1 hour's refluxing in 12% aqueous sodium hydroxide, or on 4 hours' refluxing in 6% ethanolic potassium hydroxide. Hydrolysis of the product by concentrated sulphuric acid (conditions: cf. Part VI, *loc. cit.*) gave toluene-*p*-sulphonic acid (isolated as the

S-benzylthiuronium salt) in 56—64% yields; ethanolic hydrogen chloride (conditions: cf. Part VI) afforded toluene-*p*-sulphonamide (58%) and traces of cyanuric acid.

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The Chemistry of the Pyrrocolines. Part VII. Further Experiments with 2-Methylpyrrocoline.*

By D. O. HOLLAND and J. H. C. NAYLER.

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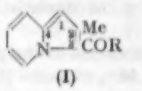
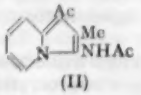
The reactions of 2-methylpyrrocoline with carbonyl chloride, benzoyl chloride, and a diazonium salt have been studied and the products orientated. Several derivatives of 2-methylpyrrocoline-3-carboxylic acid and 3-amino-2-methylpyrrocoline have been prepared. Attempted Rosenmund reduction of 2-methylpyrrocoline-3-carbonyl chloride proceeded abnormally, giving di-(2-methyl-3-pyrrocolinyl) ketone. The carbonyl group in this and other 1- or 3-acylpyrrocolines was reduced to methylene on mild treatment with lithium aluminium hydride. 3-Formyl-2-methylpyrrocoline has been prepared in high yield by the McFadyen–Stevens reaction.

THE original aims of this investigation were (*a*) to see how far certain reactions of pyrrocoline (Scholtz and Fraude, *Ber.*, 1913, **46**, 1069) could be paralleled in the case of 2-methylpyrrocoline and to orientate the products and (*b*) to prepare representatives of the then unknown class of pyrrocoline aldehydes. The description of three such aldehydes by Rossiter and Saxton (*J.*, 1953, 3654) prompted the publication of a preliminary account of some of our findings (*Chem. and Ind.*, 1954, 224).

Scholtz and Fraude (*loc. cit.*) obtained the chloride of an unidentified carboxylic acid by treating pyrrocoline with carbonyl chloride at room temperature, and 2-methylpyrrocoline has now been found to undergo a similar reaction. Treatment of the acid chloride with methylmagnesium iodide gave only a little 2-methylpyrrocoline, presumably by the action of more Grignard reagent on the acetylpyrrocoline first formed (cf. Kondo and Osawa, *J. Pharm. Soc. Japan*, 1936, **56**, 73; *Chem. Zentr.*, 1936, **107**, ii, 2910; Borrows and Holland, *J.*, 1947, 670), but with dimethylcadmium the chloride gave a fair yield of 3-acetyl-2-methylpyrrocoline (I; R = Me) identical with an authentic specimen. The carbonyl chloride reaction product can thus be formulated as 2-methylpyrrocoline-3-carbonyl chloride (I; R = Cl): Scholtz and Fraude's product was probably similarly substituted.



(I)



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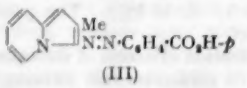


(III)

The amide (I; R = NH_2) and anilide (I; R = NHPh) were readily obtained from the chloride. In addition to the expected 2-methylpyrrocoline-3-carboxylic acid (I; R = OH) the action of cold sodium hydroxide solution on the chloride gave a larger amount of the corresponding anhydride. Perhaps because of its insolubility, the anhydride proved resistant to boiling aqueous sodium hydroxide but hot aqueous-alcoholic potassium hydroxide brought about hydrolysis to the acid. 2-Methylpyrrocoline-3-carboxylic acid is a very weak acid, being readily liberated from its sodium salt by treatment with acetic acid to pH 5—6. It is also decarboxylated with great ease: brief heating at the melting

* Part VI, *J.*, 1947, 672.

point afforded 2-methylpyrrocoline in excellent yield and the same product was obtained by warm hydrochloric acid.

Scholtz and Fraude (*loc. cit.*) obtained a benzoyl derivative by the action of cold benzoyl chloride on pyrrocoline, and 2-phenylpyrrocoline similarly afforded 3-benzoyl-2-phenylpyrrocoline (Borrows, Holland, and Kenyon, *J.*, 1946, 1069). Although 2-methylpyrrocoline did not react with acetyl chloride without a catalyst (*idem, ibid.*) reaction with benzoyl chloride has now given 3-benzoyl-2-methylpyrrocoline (I; R = Ph), the structure being proved by reduction to 3-benzyl-2-methylpyrrocoline (see below). The ketone (I; R = Ph) formed a 2 : 4-dinitrophenylhydrazone only with difficulty.

Scholtz and Fraude (*loc. cit.*) considered, on the basis of a colour reaction applicable to α-substituted pyrroles (Fischer and Bartholomaus, *Ber.*, 1912, **45**, 1919), that the red-brown dyes obtained from pyrrocoline and diazotised aromatic amines were 3-substituted pyrrocolines. Our product from 2-methylpyrrocoline and benzenediazonium chloride was a deep red oil, but use of diazotised *p*-aminobenzoic acid gave a crystalline dye. Reductive acetylation of the dye with zinc dust, acetic acid, and acetic anhydride gave a good yield of *p*-acetamidobenzoic acid together with a smaller amount of a colourless ketone, $C_{13}H_{14}O_2N_2$, which was characterised as the 2 : 4-dinitrophenylhydrazone. Oxidation of the ketone with hydrogen peroxide gave picolinic acid *N*-oxide, indicating that the substituents in the pyrrocoline nucleus were confined to the 5-membered ring, and since 1-acetamido-3-acetyl-2-methylpyrrocoline has m. p. 219° (Kondo and Nishizawa, *J. Pharm. Soc. Japan*, 1936, **56**, 1; *Chem. Abs.*, 1936, **30**, 3431) the present product, m. p. 190°, was considered to be 3-acetamido-1-acetyl-2-methylpyrrocoline (II). This indicates structure (III) for the dye and, by analogy, supports the suggested structures of Scholtz and Fraude's compounds.

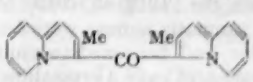
The structure of 3-acetamido-1-acetyl-2-methylpyrrocoline (II) was confirmed by an alternative synthesis. Treatment of 3-acetyl-2-methylpyrrocoline (I; R = Me) with hydrazoic acid in the presence of sulphuric acid at 0° readily gave 3-acetamido-2-methylpyrrocoline which, when heated with acetic anhydride and sodium acetate, yielded the 1-acetyl derivative (II) identical with that obtained from the dye (III). 3-Benzoyl-2-methylpyrrocoline failed to react with hydrazoic acid under the conditions which succeeded with the acetyl analogue, but prolonged treatment at room temperature gave 3-benzamido-2-methylpyrrocoline in poor yield. None of the isomeric 2-methylpyrrocoline-3-carboxyanilide, previously obtained from the acid chloride (I; R = Cl) and aniline, could be isolated. The Schmidt reaction on unsymmetrical ketones usually, but not invariably, takes place predominantly by migration of the bulkier group from carbon to nitrogen (Badger, Howard, and Simons, *J.*, 1952, 2849) and these first examples of the reaction in the pyrrocoline series follow the general tendency.

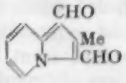
Hydrolysis of 3-acetamido-2-methylpyrrocoline by brief heating with dilute hydrochloric acid appeared to disrupt the molecule extensively since the only identifiable product was ammonium chloride. Under comparable conditions dilute phosphoric acid did not attack the amide. Hydrolysis was slowly brought about by boiling sodium hydroxide solution but the basic oil which resulted was very unstable in air and crystalline derivatives could not be prepared. The only known aminopyrrocoline, 3-acetyl-1-amino-2-methylpyrrocoline, is stated to be unstable in air (Kondo and Nishizawa, *loc. cit.*).

Attempted reduction of 2-methylpyrrocoline-3-carbonyl chloride by the Rosenmund method in boiling xylene resulted in only slow evolution of hydrogen chloride, even when unpoisoned palladised barium sulphate was used as the catalyst. Reaction in boiling anisole was faster, but in neither case was any 3-formyl-2-methylpyrrocoline (I; R = H) obtained. Instead, the product was a bright yellow solid, $C_{19}H_{16}ON_2$. It was considered that 2-methylpyrrocoline might have arisen by cleavage of the COCl group, which is known to occur in the Rosenmund reduction of certain heterocyclic acid chlorides (Mozingo and Mosettig, *Organic Reactions*, 1948, **4**, 362), and then combined with more chloride to give di-(2-methyl-3-pyrrocolinyl) ketone (IV). This was supported by production of the compound $C_{19}H_{16}ON_2$, albeit in low yield, when the acid chloride was refluxed in anisole under nitrogen. Apparently some 2-methylpyrrocoline is formed merely by thermal decomposition of the chloride, but the reducing conditions of the Rosenmund reaction are doubtless

more favourable for the production of the supposed intermediate. Formation of the presumed di-(2-methyl-3-pyrrocolinyl) ketone in high yield when 2-methylpyrrocoline was heated with the acid chloride in benzene provided still stronger support for the suggested mechanism. There is no proof of the attachment of the carbonyl group to the 3-position of both pyrrocoline nuclei, but this is the usual site of attack by acid chlorides.

In common with other acylpyrrocolines the ketone (IV) was decomposed by hot mineral acid, the yield of 2-methylpyrrocoline being virtually quantitative. The substance failed to react with the usual carbonyl reagents even on prolonged heating, but this is not surprising in view of the considerable steric hindrance and the known low reactivity of acetyl and benzoyl groups in the 3-position of the pyrrocoline nucleus.

(IV) 



(V)

With the object of substantiating the presence of the keto-group, reduction of (IV) to a secondary alcohol was attempted. The compound was not attacked by zinc dust and hot alcoholic potassium hydroxide or acetic acid or by aluminium or sodium *iso*propoxides in boiling xylene. Sodium borohydride in boiling methanol was also ineffective, but lithium aluminium hydride in ether effected rapid reduction at ordinary temperature. The product, however, was not an alcohol but di-(2-methyl-3-pyrrocolinyl)methane, which was also obtained from 2-methylpyrrocoline and formaldehyde at room temperature, thus providing further support for the symmetrical structure of the ketone (IV). Scholtz (*Ber.*, 1912, **45**, 734) reported the condensation of various aromatic aldehydes with pyrrocoline and suggested by analogy with the β-reactivity of indole, that reaction probably occurred in one of the β-(*i.e.*, 1- and 2-)positions of the pyrrocoline ring, but since the 3-position is now known to be the most reactive centre his products also were probably di-3-pyrrocolinylmethanes.

As in the case of the ketone (IV), treatment of 3-acetyl- and 3-benzoyl-2-methylpyrrocoline with lithium aluminium hydride caused elimination of oxygen and the high yields and absence of side-reactions make this method of reduction distinctly preferable to the Wolff–Kishner or modified Clemmensen procedures which have been used hitherto (Borrows, Holland, and Kenyon, *J.*, 1946, 1083). In order to determine whether a typical 1-acylpyrrocoline would be reduced in the same way, 1-acetyl-2 : 3-dimethylpyrrocoline was prepared by the action of acetic anhydride and sodium acetate on 2 : 3-dimethylpyrrocoline. The resulting ketone was characterised as the oxime, and the presence of the substituent in the only free position of the 5-membered ring was established by oxidation to picolinic acid *N*-oxide. Mild treatment of the ketone with lithium aluminium hydride gave 1-ethyl-2 : 3-dimethylpyrrocoline.

Rossiter and Saxton (*loc. cit.*) later reported the formation of 1 : 2 : 3-trimethylpyrrocoline by the action of lithium aluminium hydride on 1-formyl-2 : 3-dimethylpyrrocoline and indeed complete elimination of oxygen from a group attached to a position of high electron density is now known to be not unusual (cf. Conover and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 3586), although only in the case of certain 3-indolyl derivatives (Leete and Marion, *Canad. J. Chem.*, 1953, **31**, 775) has it been observed under conditions as mild as those which suffice for 1- and 3-acylpyrrocolines.

When the Rosenmund reaction failed to yield 3-formyl-2-methylpyrrocoline a possible synthesis similar to that of 3-formylindole by Elks, Elliott, and Hems (*J.*, 1944, 629) was considered. 2-Methylpyrrocoline did not condense with ethyl oxalate under the conditions which succeed with indole, but treatment with ethoxalyl chloride readily gave a crystalline product which, by analogy with the behaviour of other acid chlorides, was considered to be ethyl 2-methylpyrrocoline-3-glyoxylate (I; R = CO_2Et). Alkaline hydrolysis then gave the acid (I; R = CO_2H), but attempts to convert this into the anil merely gave the aniline salt. The failure of other efforts to protect the carbonyl group in (I; R = CO_2H or CO_2Et) and of attempts to decarboxylate the unprotected keto-acid caused this approach to be abandoned.

Finally, 2-methylpyrrocoline-3-carbonyl chloride was treated with hydrazine, and the benzenesulphonyl derivative of the resulting hydrazide (I; R = $NH{\cdot}NH_2$) was heated with

sodium carbonate in ethylene glycol according to the general procedure of McFadyen and Stevens (*J.*, **1936**, **584**), to give a good yield of 3-formyl-2-methylpyrrocoline. Rossiter and Saxton (*loc. cit.*) obtained this aldehyde in poor yield by the action of *N*-methylformanilide and phosphorus oxychloride on 2-methylpyrrocoline, but under essentially similar conditions we isolated only a little 1 : 3-diformyl-2-methylpyrrocoline (V). As in the preparation of 3-formylindole (Tyson and Shaw, *J. Amer. Chem. Soc.*, **1952**, **74**, **2273**), substitution of dimethylformamide for *N*-methylformanilide increased the yield of dialdehyde. Rossiter and Saxton (*loc. cit.*) prepared the dialdehyde by the Reimer–Tiemann reaction and characterised it as the monophenylhydrazone. We have found that the action of hydroxylamine or 2 : 4-dinitrophenylhydrazine in excess similarly involves only one carbonyl group, thus recalling the behaviour of 1 : 3-diacetylpyrrocolines (Borrows, Holland, and Kenyon, *J.*, **1946**, **1069**).

Experimental

2-Methylpyrrocoline-3-carbonyl Chloride.—2-Methylpyrrocoline (30·7 g.) in toluene (120 ml.) was added with cooling and stirring to a 12·5% solution (180 ml.) of carbonyl chloride in toluene, at $<15°$. Next morning, the dark deliquescent precipitate of crude 2-methylpyrrocoline hydrochloride was removed and the filtrate was evaporated *in vacuo*. The residue was extracted with boiling light petroleum (270 ml.; b. p. 60—80°) and the extracts were cooled to give pale green needles of *2-methylpyrrocoline-3-carbonyl chloride* (25·0 g.), m. p. 68—69°. This was sufficiently pure for most purposes but recrystallised (with considerable loss) from light petroleum forming lemon-yellow needles, m. p. 73° (Found: C, 61·9; H, 4·2; N, 7·4; Cl, 18·5. $C_{10}H_8ONCl$ requires C, 62·0; H, 4·2; N, 7·2; Cl, 18·3%). The product was stable for 2—3 weeks at 0°. The yield was not increased by the inclusion of pyridine.

Reaction of 2-Methylpyrrocoline-3-carbonyl Chloride with Dimethylcadmium.—A stirred solution of dimethylcadmium in ether (from 10 g. of anhydrous cadmium chloride) was treated with 20 ml. of a solution prepared from the pure acid chloride (10 g.) and dry ether (120 ml.). After warming to initiate the reaction the source of heat was removed and the remainder of the acid chloride solution was added during 30 min. so as to maintain gentle reflux. After being kept overnight the mixture was treated with crushed ice, followed by 5*N*-sulphuric acid (40 ml.), and filtered. The solid was discarded after being washed with water and ether. The aqueous phase of the filtrate was neutralised with sodium carbonate and extracted with ether, and the combined ether solutions were washed with dilute sodium hydroxide solution, then with water, and dried. Removal of the ether left crude 3-acetyl-2-methylpyrrocoline as a yellow-green solid (4·33 g., 48%), which crystallised from light petroleum (charcoal) in stout cream-coloured needles, m. p. 83° not depressed by admixture with an authentic specimen (Borrows, Holland, and Kenyon, *J.*, 1946, 1069) (Found: C, 76·7; H, 6·8; N, 8·4. Calc. for $C_{11}H_{11}ON$: C, 76·3; H, 6·4; N, 8·1%). The 2 : 4-dinitrophenylhydrazone had m. p. and mixed m. p. 253° (slight decomp.).

2-Methylpyrrocoline-3-carboxyamide.—A suspension of 2-methylpyrrocoline-3-carbonyl chloride (6 g.) in aqueous ammonia (*d* 0·88; 60 ml.) was shaken for 2 hr., set aside overnight, and filtered. The light green solid (4·51 g.) crystallised from ethyl acetate (charcoal) as colourless needles of the *amide*, m. p. 185—187° (Found: C, 69·3; H, 6·1; N, 16·6. $C_{10}H_{10}ON_2$ requires C, 69·0; H, 5·8; N, 16·1%).

2-Methylpyrrocoline-3-carboxyanilide.—A solution of the acid chloride (3 g.) and aniline (4 ml.) in benzene (25 ml.) was heated on the steam-bath for 45 min., then poured into water. The light green solid was collected and concentration of the benzene layer furnished a further quantity (combined yield 3·04 g.). The *anilide* crystallised from alcohol (charcoal) in colourless needles, m. p. 142—143° (Found: C, 77·1; H, 5·8; N, 11·6. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%).

Hydrolysis of 2-Methylpyrrocoline-3-carbonyl Chloride.—A suspension of the acid chloride (16 g.) in 10% sodium hydroxide solution (180 ml.) was shaken for 90 min. and filtered. Crystallisation of the solid (7·56 g., 55%) from chloroform–ether and finally from ethyl acetate (charcoal) gave the pale lemon-yellow *anhydride*, m. p. 203—204° (Found: C, 72·7; H, 5·0; N, 8·2. $C_{20}H_{14}O_3N_2$ requires C, 72·3; H, 4·8; N, 8·4%).

The aqueous filtrate was treated with acetic acid (27 ml.) and *2-methylpyrrocoline-3-carboxylic acid* was collected, washed with water, and dried as rapidly as possible between filter papers and finally in a vacuum-desiccator to give 4·09 g. (28%) of an olive-coloured powder. (The finely divided acid was difficult to filter and the crude moist product tended to undergo spontaneous

decarboxylation during drying. Alternatively the acid could be extracted into ether and dried over anhydrous sodium sulphate.) Crystallisation from ether–light petroleum gave colourless crystals, m. p. 115° (vigorous decomp.) (Found : C, 68·5; H, 5·3; N, 8·2. $C_{10}H_9O_2N$ requires C, 68·5; H, 5·2; N, 8·0%).

Hydrolysis of 2-Methylpyrrocoline-3-carboxylic Anhydride.—A mixture of the anhydride (3 g.), ethanol (40 ml.), and 50% aqueous potassium hydroxide (20 ml.) was refluxed for 1 hr., then concentrated to remove alcohol and diluted with water. Addition of acetic acid precipitated crude 2-methylpyrrocoline-3-carboxylic acid (2·68 g., 85%) which, after purification as described above, had m. p. and mixed m. p. 115° (vigorous decomp.).

Decarboxylation of 2-Methylpyrrocoline-3-carboxylic Acid.—(*a*) The pure acid (0·35 g.) decomposed rapidly at 130°/14 mm. After 20 min. colourless crystalline 2-methylpyrrocoline (0·21 g., 80%) which had sublimed was removed; it had m. p. and mixed m. p. 59°. (*b*) A solution of the acid (0·4 g.) in concentrated hydrochloric acid (5 ml.) was kept at 60° for 30 min., then poured into cold sodium hydroxide solution. The precipitated base (0·25 g., 85%) had m. p. 56—57°, raised to 59° (mixed m. p.) by sublimation.

3-Benzoyl-2-methylpyrrocoline.—A mixture of 2-methylpyrrocoline (20 g.) and benzoyl chloride (25 ml.) in benzene (50 ml.) was set aside overnight, then poured into sodium hydroxide solution. A little 2-methylpyrrocoline was removed by steam-distillation and the residue extracted with chloroform. Evaporation of the extracts left a dark oil which was rubbed with light petroleum containing a little ether to give a yellow-green powder (33·1 g.). *3-Benzoyl-2-methylpyrrocoline* crystallised from light petroleum in flat yellow needles, m. p. 63° (Found : C, 81·7; H, 5·9; N, 5·6. $C_{16}H_{13}ON$ requires C, 81·6; H, 5·6; N, 6·0%).

The ketone (0·5 g.) and 2 : 4-dinitrophenylhydrazine (0·5 g.) in ethanol (50 ml.) containing concentrated hydrochloric acid (0·5 ml.) were refluxed for 90 min. The *hydrazone* (0·17 g.) which separated on cooling was dissolved in hot pyridine and the blood-red solution was concentrated to about 6 ml. and diluted with hot alcohol (6 ml.) to give black crystals, m. p. 288—290° (decomp.) (Found : C, 63·7; H, 4·0; N, 16·6. $C_{22}H_{17}O_4N_5$ requires C, 63·6; H, 4·1; N, 16·9%).

3-p-Carboxyphenylazo-2-methylpyrrocoline (III).—Diazotised *p*-aminobenzoic acid (5·48 g.), brought to pH 8 by sodium hydroxide solution, was added to a solution of 2-methylpyrrocoline (5·24 g.) in ethanol (120 ml.). After dilution with 10% aqueous acetic acid (220 ml.) the crimson solid was collected and thoroughly washed with water and ether. The *dye* (10·6 g., 95%) had m. p. 249° (decomp.), unchanged on crystallisation from 2-ethoxyethanol (Found : C, 68·7; H, 5·0; N, 14·8. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%).

Reductive Acetylation of the Dye (III).—A solution of the dye (5 g.) in acetic acid (100 ml.) and acetic anhydride (100 ml.) was boiled for 20 min. whilst zinc dust (10 g.) was added portionwise, and then for 10 min. more. The brown mixture was cooled and filtered, and the solid was washed with acetic acid. The filtrate and washings were evaporated *in vacuo*, the residual tar was treated with sodium hydroxide solution, and the mixture was extracted with chloroform. Acidification of the aqueous layer gave crude *p*-acetamidobenzoic acid (2·60 g., 81%), m. p. and mixed m. p. 252°. The dark chloroform solution was dried, concentrated to about 20 ml., diluted with benzene (60 ml.), and chromatographed on alumina. The chromatogram was developed with benzene–acetone and the eluate from the leading cream-coloured band was evaporated to an oil, which crystallised on trituration with ether. The solid (0·24 g.) crystallised from ethyl acetate to give colourless silky needles of *3-acetamido-1-acetyl-2-methylpyrrocoline*, m. p. 190° (Found : C, 67·5; H, 6·2; N, 12·2. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1; N, 12·2%). Treatment of a methanolic solution of the ketone with Brady's reagent gave the purple-black *2 : 4-dinitrophenylhydrazone*, which separated from 2-ethoxyethanol in needles, m. p. 265° (Found : C, 55·5; H, 4·5. $C_{19}H_{18}O_5N_6$ requires C, 55·6; H, 4·4%).

Oxidation of 3-Acetamido-1-acetyl-2-methylpyrrocoline.—A mixture of the pyrrocoline (0·25 g.), acetic acid (6 ml.), and 30% hydrogen peroxide (3 ml.) was refluxed for 1 hr. and evaporated *in vacuo*. The residual colourless syrup was dried in a vacuum-desiccator, then triturated with a little dry methanol to give picolinic acid *N*-oxide (0·04 g.), m. p. and mixed m. p. 161°.

3-Acetamido-2-methylpyrrocoline.—A solution of 3-acetyl-2-methylpyrrocoline (12·8 g.) in chloroform (50 ml.) was treated with hydrazoic acid in chloroform (100 ml. of 3·44% w/v) and added dropwise during 30 min. to vigorously stirred concentrated sulphuric acid (40 ml.) and chloroform (80 ml.) at −5° to 0°. After being stirred for a further 30 min. at the same temperature the mixture was poured on ice and made alkaline with 40% aqueous sodium hydroxide. The layers were separated, the aqueous phase was extracted with chloroform, and the combined chloroform solutions were dried and evaporated. Trituration of the sticky residue with ether gave crude *3-acetamido-2-methylpyrrocoline* (9·56 g., 69%), which crystallised from benzene in

colourless hair-like needles, m. p. 148° (Found: C, 70·3; H, 6·8; N, 14·3. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%).

Acetylation of 3-*Acetamido*-2-*methylpyrrocoline.*—The pyrrocoline (1·88 g.), acetic anhydride (15 ml.), and anhydrous sodium acetate (3 g.) were refluxed for 3 hr., and evaporated *in vacuo*. The residue was treated with sodium hydroxide solution and extracted with chloroform. Evaporation of the dried extracts and trituration of the residue with ether gave a very crude solid, which on crystallisation from ethyl acetate (charcoal) gave 0·30 g. of fairly pure 3-acetamido-1-acetyl-2-methylpyrrocoline, m. p. 187—188°. Further crystallisation raised the m. p. to 190°, not depressed by admixture with the product from the reductive acetylation of the dye (III).

3-*Benzamido*-2-*methylpyrrocoline.*—A solution of 3-benzoyl-2-methylpyrrocoline (3·2 g.) in chloroform (20 ml.) was treated with hydrazoic acid in the same solvent (24 ml. of 3·07% w/v) and the mixture was added dropwise with stirring during 30 min. to concentrated sulphuric acid (10 ml.) and chloroform (20 ml.) at 0—10°. After 27 hours' stirring at room temperature the mixture was poured on ice, the aqueous layer was extracted with chloroform, and the combined chloroform solutions were dried and evaporated. Rubbing the residual gum with a little cold acetone gave a yellow-brown solid (2·18 g., m. p. about 160°) which, however, could not be purified by recrystallisation. A solution of the solid (2 g.) in chloroform (50 ml.) was diluted with benzene (100 ml.) and chromatographed on alumina. The leading yellow band was eluted with chloroform–benzene (1 : 2) and the solvent was removed to leave crude 3-*benzamido*-2-*methylpyrrocoline* (0·35 g.), pale yellow crystals (from benzene), m. p. 196° (Found: C, 76·8; H, 5·7; N, 11·5. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%). Elution of the remaining bands from the alumina column gave only tars.

Attempted Rosenmund Reduction of 2-*Methylpyrrocoline*-3-*carbonyl Chloride.*—Dry hydrogen was passed into a vigorously stirred solution of the acid chloride (7·5 g.) in boiling xylene (130 ml.) in the presence of 5% palladised barium sulphate until, after 16½ hr., evolution of hydrogen chloride ceased at 89% of the theoretical quantity. After cooling in a stream of hydrogen, the mixture was filtered and the solvent was removed *in vacuo*. Trituration of the residual deep red gum with light petroleum containing a little ether gave crude *di*-(2-*methyl*-3-*pyrrocolinyl*) *ketone* (3·74 g.) which crystallised from alcohol or light petroleum in elongated yellow plates, m. p. 114—115° (Found: C, 79·1; H, 6·2; N, 10·0. $C_{19}H_{16}ON_2$ requires C, 79·1; H, 5·6; N, 9·7%). Neither distillation of the mother-liquor *in vacuo* nor treatment with Brady's reagent gave any evidence of the presence of 3-formyl-2-methylpyrrocoline.

Di-(2-*methyl*-3-*pyrrocolinyl*) *Ketone.*—A solution of 2-methylpyrrocoline-3-carbonyl chloride (4·54 g.) and 2-methylpyrrocoline (6·15 g.) in benzene (80 ml.) was refluxed under nitrogen for 14 hr. and evaporated *in vacuo* to a dark oil. Sodium hydroxide solution was added, 2-methylpyrrocoline was removed by steam-distillation, and the residual mixture was extracted with ether. The washed and dried extracts were treated with charcoal and evaporated to a gum, which gave the ketone (4·73 g., 70%) when rubbed with light petroleum containing a little ether. Recrystallisation from ethanol gave a product, m. p. 114—115°, identical with that from the attempted Rosenmund reaction.

Hydrolysis of Di-(2-*methyl*-3-*pyrrocolinyl*) *Ketone.*—The ketone (1 g.) in concentrated hydrochloric acid (10 ml.) was heated on the steam-bath for 1 hr., cooled, and poured into an excess of sodium carbonate solution. Steam-distillation gave 0·9 g. of crude 2-methylpyrrocoline, m. p. 54—55°, raised to 59° (mixed m. p.) by sublimation.

Di-(2-*methyl*-3-*pyrrocolinyl*)*methane.*—(*a*) The ketone (IV) (2 g.) in ether (50 ml.) was added during 30 min. to a stirred suspension of lithium aluminium hydride (0·4 g.) in ether (50 ml.) at room temperature, the brilliant yellow colour of the ketone disappearing at once at each addition. Water (5 ml.) and 40% sodium hydroxide solution (20 ml.) were added and the layers were separated (decomposition of the complex with mineral acid was best avoided since it gave an intense indigo colour). The aqueous phase was extracted with chloroform and the combined solvent layers were dried and evaporated. Crystallisation of the green residue from ethyl acetate (charcoal) gave small colourless prisms of *di*-(2-*methyl*-3-*pyrrocolinyl*)*methane* (1·42 g., 75%), m. p. 159—161° (Found: C, 83·1; H, 6·5; N, 10·3. $C_{19}H_{18}N_2$ requires C, 83·2; H, 6·6; N, 10·2%).

(*b*) Aqueous formaldehyde (40%; 0·5 ml.) was added to 2-methylpyrrocoline (1 g.) in ethanol (10 ml.) and next morning di-(2-methyl-3-pyrrocolinyl)methane (0·99 g., 95%) was collected and crystallised from ethyl acetate (charcoal); it had m. p. and mixed m. p. 159—160°.

3-*Ethyl*-2-*methylpyrrocoline.*—3-Acetyl-2-methylpyrrocoline (8·3 g.) was reduced with lithium aluminium hydride (3 g.) as described for the reduction of the ketone (IV) except that the ether solution was refluxed for 100 min. 3-Ethyl-2-methylpyrrocoline (5·81 g., 76%) was isolated by

ether-extraction and distilled; it had b. p. 116—118°/9 mm., n_D^{15} 1·5973 [chloroplatinate, m. p. 174° (decomp.) (Found : C, 36·7; H, 4·2; Cl, 29·2. Calc. for $C_{22}H_{36}N_2Cl_6Pt$: C, 36·3; H, 3·9; Cl, 29·2%)]. Borrows, Holland, and Kenyon (*J.*, 1946, 1083) give b. p. 124°/15 mm., n_D^{20} 1·5968 [chloroplatinate, m. p. 174° (decomp.)].

3-Benzyl-2-methylpyrrocoline.—3-Benzoyl-2-methylpyrrocoline (7·05 g.) was reduced with lithium aluminium hydride (2·5 g.) as described above, to give 3-benzyl-2-methylpyrrocoline (4·02 g., 61%), m. p. 86—88° raised to 93—94° by sublimation at 0·1 mm. and not depressed by admixture with an authentic specimen (Holland and Nayler, *J.*, 1955, in the press). The chloroplatinate had m. p. and mixed m. p. 178—179° (decomp.).

1-Acetyl-2 : 3-dimethylpyrrocoline.—2 : 3-Dimethylpyrrocoline (29 g.), acetic anhydride (180 ml.), and anhydrous sodium acetate (30 g.) were refluxed for 7 hr. and evaporated *in vacuo*. After addition of water the dark mixture was extracted with chloroform and the washed and dried extracts were distilled, to give *1-acetyl-2 : 3-dimethylpyrrocoline* (18·6 g., 50%) as a green oil, b. p. 130—140°/0·1 mm., which solidified. The ketone crystallised from light petroleum in colourless needles, m. p. 81—82° (Found : C, 77·4; H, 7·4; N, 7·9. $C_{13}H_{13}ON$ requires C, 77·0; H, 7·0; N, 7·5%). Heating the ketone with hydroxylamine hydrochloride and sodium acetate in aqueous alcohol gave the *oxime*, pale yellow prisms (from ethyl acetate), m. p. 216° (decomp.) (Found : C, 71·7; H, 6·9; N, 13·5. $C_{13}H_{14}ON_2$ requires C, 71·3; H, 7·0; N, 13·9%). Oxidation of the ketone (0·25 g.) with 100-vol. hydrogen peroxide, as described for 3-acetamido-1-acetyl-2-methylpyrrocoline, gave picolinic acid *N*-oxide (0·04 g.).

1-Ethyl-2 : 3-dimethylpyrrocoline.—1-Acetyl-2 : 3-dimethylpyrrocoline (10 g.) was reduced with lithium aluminium hydride (3 g.) as before, to give *1-ethyl-2 : 3-dimethylpyrrocoline* (6·2 g., 67%) as a yellow oil, b. p. 91—92°/0·2 mm. (Found : C, 82·6; H, 8·6; N, 8·1. $C_{12}H_{15}N$ requires C, 83·2; H, 8·7; N, 8·1%). The insoluble *chloroplatinate* formed golden needles, m. p. 177—178° (decomp.) (Found : C, 38·4; H, 4·2; Pt, 25·6. $C_{24}H_{32}N_2Cl_6Pt$ requires C, 38·1; H, 4·3; Pt, 25·8%).

Ethyl 2-Methylpyrrocoline-3-glyoxylate.—A mixture of ethoxalyl chloride (Adickes, Brunnert, and Lücker, *J. prakt. Chem.*, 1931, **130**, 169) (12·5 g.) and 2-methylpyrrocoline (12 g.) in benzene (120 ml.) was kept at ordinary temperature overnight (or, alternatively, refluxed for 30 mins.) and poured into ice-water. The aqueous phase was extracted with chloroform and the combined organic solutions were washed and dried. Removal of the solvents and crystallisation of the dark residue from alcohol (charcoal) gave the yellow-green *ester* (14·1 g., 67%). Further crystallisation gave pale yellow elongated plates, m. p. 105—106° (Found : C, 67·7; H, 6·3; N, 6·1. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·7; N, 6·1%).

2-Methylpyrrocoline-3-glyoxylic Acid.—A suspension of the ester (15 g.) in 2N-sodium hydroxide (150 ml.) was shaken overnight, then heated at 70° for 30 min. The dark solution was decolorised with charcoal and made strongly acid with hydrochloric acid, to give a precipitate (12·3 g., 93%), m. p. 148—150° (decomp.). The *acid* crystallised from chloroform–light petroleum in greenish-yellow prisms, m. p. 151° (decomp.) (Found : C, 64·9; H, 4·7; N, 6·9. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·5; N, 6·9%).

A suspension of the acid (6 g.) and aniline (3 g.) in water (60 ml.) was heated on the steam-bath for 30 min. and cooled, whereupon the *aniline salt* crystallised (5·73 g.). Recrystallisation from alcohol gave bold yellow-green needles, m. p. 149—150° (decomp.) (Found : C, 69·0; H, 5·5; N, 9·5. $C_{17}H_{16}O_3N_2$ requires C, 68·9; H, 5·4; N, 9·5%). The product was not the anil since on dissolution in sodium hydrogen carbonate solution aniline was liberated (extracted with ether and identified as acetanilide), whilst acidification of the aqueous layer precipitated the glyoxylic acid.

3-Methylpyrrocoline-3-carboxyhydrazide.—A solution of 2-methylpyrrocoline-3-carbonyl chloride (25 g.) in ether (500 ml.) was added during 1 hr. to a stirred mixture of 90% hydrazine hydrate (80 ml.) and ethanol (500 ml.) kept at 0—10°. After storage at 0° overnight the colourless crystals were collected and thoroughly washed with water and ether (15·6 g., m. p. 171—173°). Evaporation of the filtrate *in vacuo* gave a further 5·7 g., m. p. 167—169° (total yield 87%). The *hydrazide* crystallised from ethyl acetate as colourless glistening rectangular plates, m. p. 171—172° (Found : C, 63·8; H, 6·0; N, 22·5. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·9; N, 22·2%).

3-Formyl-2-methylpyrrocoline.—Benzenesulphonyl chloride (19·2 ml.) was added during 30 min. to a stirred suspension of the hydrazide (23·1 g.) in pyridine (150 ml.) at −5° to 0°, and the mixture was then stirred at room temperature for 90 min. The turbid orange solution was poured on crushed ice, the crude yellow *benzenesulphonyl derivative* was collected and washed first with dilute hydrochloric acid, then with water, and dried in a vacuum-desiccator [36·5 g.

(91%); m. p. 177—178° (decomp.)]. It crystallised from acetonitrile in cream-coloured needles, m. p. 183—184° (decomp.) (Found: C, 58·3; H, 4·7; N, 13·1. $C_{16}H_{16}O_3N_2S$ requires C, 58·3; H, 4·6; N, 12·8%).

The crude intermediate (36·5 g.) in ethylene glycol (250 ml.) was heated in an oil-bath and when the internal temperature reached 140° anhydrous sodium carbonate (20 g.) was added in several portions during 1 min. Evolution of nitrogen was vigorous, but subsided rapidly. After a further 2 min. at 140—145° the solution was diluted with hot water (250 ml.), cooled, and poured into a further 500 ml. of water. The mixture was extracted with ether (3 × 150 ml.), and the extracts were dried (Na_2SO_4) and distilled. 3-Formyl-2-methylpyrrocoline, b. p. 102—107°/0·3 mm., crystallised in the receiver (yield 13·6 g., 77%) and sublimation *in vacuo* gave pale yellow crystals, m. p. 56° (Found: C, 75·0; H, 5·9; N, 9·2. Calc. for $C_{10}H_9ON$: C, 75·4; H, 5·7; N, 8·8%).

Addition of Brady's reagent to the aldehyde in methanol gave the sparingly soluble 2 : 4-*dinitrophenylhydrazone*. The intense blood-red solution of this derivative in hot pyridine deposited almost black needles, m. p. 267° (decomp.), when cooled (Found: C, 59·0; H, 4·4; N, 20·4. $C_{16}H_{12}O_4N_5,0{\cdot}5C_5H_5N$ requires C, 58·7; H, 4·1; N, 20·3%). Rossiter and Saxton (*loc. cit.*) were unable to purify this derivative from ethyl acetate.

1 : 3-*Diformyl-2-methylpyrrocoline.*—Phosphorus oxychoride (20 ml.) was gradually added with stirring to dimethylformamide (80 ml.) below 10°, after which 2-methylpyrrocoline (12 g.) was added portionwise during 10 min. while the temperature rose to 30°. After the mixture had been stirred for 30 min. at 25—30° calcium carbonate (40 g.) was added during 5 min. and the mixture was warmed cautiously. When a vigorous reaction set in the mixture was cooled strongly to keep it at 55—60° until after 5 min. the reaction subsided. After a further 10 min. at 50° the mixture, which now contained much solid, was cooled to 10°, treated with stirring with sodium acetate trihydrate (85 g.) in water (200 ml.), and set aside overnight. The dark green suspension was then poured into 6% sodium hydroxide solution (800 ml.), boiled for 2 hr. to expel dimethylamine, and filtered hot. The solid was thoroughly extracted with boiling chloroform and the filtrate was extracted with the cold solvent. The combined extracts (600 ml.) were dried and evaporated, and the sticky residue was washed with ether to give crude 1 : 3-diformyl-2-methylpyrrocoline (4·84 g., 28%), m. p. 209—212°. Crystallisation from alcohol (charcoal) gave colourless needles, m. p. 214—215° not depressed by admixture with the product of the Reimer–Tiemann reaction (Rossiter and Saxton, *loc. cit.*) (Found: C, 70·7; H, 5·2; N, 7·2. Calc. for $C_{11}H_9O_2N$: C, 70·6; H, 4·9; N, 7·5%). Rossiter and Saxton describe the dialdehyde as pale yellow needles, m. p. 210°.

Hydrogen peroxide oxidised the dialdehyde (0·5 g.) to picolinic acid *N*-oxide (0·21 g.).

Solutions of the dialdehyde (0·3 g.) in hot ethanol (25 ml.) and of hydroxylamine hydrochloride (0·3 g.) and sodium acetate trihydrate (0·5 g.) in water (15 ml.) were mixed and set aside overnight to give the *mono-oxime* (0·18 g.), which crystallised from 33% aqueous alcohol in pale yellow needles, m. p. 196—197° (Found: C, 65·3; H, 5·2; N, 14·2. $C_{11}H_{10}O_2N_2$ requires C, 65·3; H, 5·0; N, 13·9%). Addition of Brady's reagent (1 mol. or excess) to the dialdehyde in methanol gave the insoluble red-brown *mono*-2 : 4-*dinitrophenylhydrazone*, decomp. >315° (Found: C, 55·0; H, 3·7; N, 19·2. $C_{17}H_{12}O_5N_6$ requires C, 55·5; H, 3·6; N, 19·1%).

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Stereochemical Studies of Olefinic Compounds. Part IV. The Configuration of "Leaf Alcohol" and a Further Synthesis of* cis*-Jasmone.*

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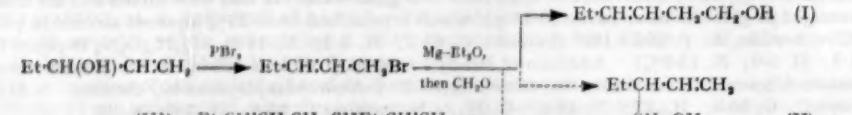
It is shown that the Grignard reagent from *trans*-pent-2-enyl bromide reacts with formaldehyde to give 2-ethylbut-3-en-1-ol and no hex-3-en-1-ol. The recent criticism by Obata and Morito of the assignment of configuration made in Part I to "leaf alcohol" (*cis*-hex-3-en-1-ol) and related compounds is thereby negatived.

It is shown that the hydrocarbon formed by Wurtz–Grignard coupling of *trans*-pent-2-enyl bromide results from reaction between the unrearranged halide and the rearranged secondary form of the Grignard reagent.

Stereochemically pure *cis*-jasmone is synthesised in five stages from synthetic "leaf alcohol", *via cis*-oct-5-en-2-one; this constitutes the shortest synthesis so far devised.

In Part I of this series (*J.*, 1950, 873) Crombie and Harper put forward, what were believed to be, cogent arguments establishing "leaf alcohol" as *cis*-hex-3-en-1-ol. From this similar (*cis*-)configurations were deduced for "violet-leaf aldehyde" and natural jasmone (*idem*, *Perfumery Essent. Oil Record*, 1950, **41**, 197), subsequently confirmed for the latter by synthesis (*idem*, *J.*, 1952, 869). Obata and Morito (*J. Agric. Chem. Soc. Japan*, 1951, **25**, 210), however, have criticised these deductions and proposed again the *trans*-configurations for these substances. They supported their argument by what purports to be a new synthesis of *trans*-hex-3-en-1-ol. They stated that the 3 : 5-dinitrobenzoate of their product "is identical with that of natural leaf-alcohol in having m. p. 49·5—50° Hence the stereo-form of natural leaf-alcohol is *trans*." The claim for identity is based upon the correspondence of melting points rather than upon an actual mixed melting point. This point is relevant for it was shown in Part I that, although the 3 : 5-dinitrobenzoate of authentic *trans*-hex-3-en-1-ol does have the same melting point as that of "leaf alcohol," on admixture a marked depression is obtained.

The key stages of Obata and Morito's reaction scheme are (solid arrows):



Whilst agreeing with Obata and Morito that interaction of pent-1-en-3-ol with phosphorus tribromide would give *trans*-pent-2-enyl bromide through allylic rearrangement, we would, on the contrary, expect the Grignard reagent from this bromide to react with formaldehyde largely, if not completely, through a second allylic rearrangement to give, not *trans*-hex-3-en-1-ol (I), but the hitherto undescribed 2-ethylbut-3-en-1-ol (II). There is a close parallel for this expectation in that Roberts and Young [*J. Amer. Chem. Soc.*, 1945, **67**, 148; cf. Ou Kiun Houo, *Ann. Chim.* (*France*), 1940, **13**, 175] have shown the Grignard reagent from *trans*-but-2-enyl bromide reacts with formaldehyde to give 2-methylbut-3-en-1-ol exclusively.

To clarify the situation we have repeated Obata and Morito's synthesis. The product from the interaction of the Grignard reagent of *trans*-pent-2-enyl bromide with formaldehyde did not possess the "leaf alcohol" odour and had a boiling point (136—137°) 20° below that of the hex-3-en-1-ols, as is to be expected if it is a branched-chain isomer. Although the crude 3 : 5-dinitrobenzoate of the product had the same melting point as that of both *cis*-

* Part III, *J.*, 1950, 1715.

and *trans*-hex-3-en-1-ol (48—49°), recrystallisation raised it slightly (to 53°). The lack of identity of this 3 : 5-dinitrobenzoate with that of either *cis*- or *trans*-hex-3-en-1-ol was strikingly demonstrated on admixture, a depression of the melting point occurring sufficient to cause liquefaction from the warmth of the fingers. Lack of identity was further shown by the 4-diphenylylurethane, whose melting point (79°) was distinct from that of either the *cis*- (91°) or the *trans*-hex-3-en-1-ol (99°) derivative. The product of this synthesis, therefore, is neither *cis*- (" leaf alcohol ") nor *trans*-hex-3-en-1-ol and consequently the argument of Obata and Morito is negatived.

Although the alcoholic product gave analytically satisfactory derivatives it had persistently far too high a carbon content. This was traced to the presence of hydrocarbon, presumably formed by Wurtz–Grignard coupling of the allylic halide, whose identity is considered below. Separation was achieved through the hydrogen phthalate which then gave analytically satisfactory alcohol but of otherwise unchanged properties. Confirmation that the alcohol is 2-ethylbut-3-en-1-ol followed from catalytic hydrogenation (uptake equivalent to 1·00 double bond) to 2-ethylbutanol, identified as the 3 : 5-dinitrobenzoate, and from the infrared absorption spectrum : strong bands were present at 10·06 and 10·96 μ, due to ·CH:CH_2, and at 9·61 μ, due to ·CH_2·OH, whilst absorption at 10·31 μ was negligible, showing the absence of *trans*-CH:CH.

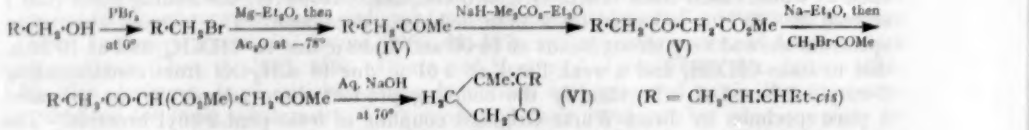
Only a small amount of the hydrocarbon contaminant, not entirely free from alcohol, was isolated, but analysis and quantitative hydrogenation suggested that it was a decadiene, such as would result from Wurtz–Grignard coupling. However, the boiling point (130°) seemed 20—30° too low even for a branched-chain decadiene. The infrared absorption spectrum showed very strong bands at 10·06 and 10·98 μ, due to ·CH:CH_2, and at 10·36 μ, due to *trans*-CH:CH, and a weak band at 9·61 μ, due to ·CH_2·OH from contaminating 2-ethylbut-3-en-1-ol. To identify the coupling product more adequately we prepared a pure specimen by direct Wurtz–Grignard coupling of *trans*-pent-2-enyl bromide. The hydrocarbon now had the expected boiling point (155°) and microhydrogenation gave an uptake equivalent to 1·95 double bonds, whilst the infrared absorption spectrum again showed the (equally) strong bands due to ·CH:CH_2 and *trans*-CH:CH. The hydrocarbon is, therefore, *trans*-3-ethylocta-1 : 5-diene (III). The elucidation of its structure provides further confirmation that in the Wurtz–Grignard coupling of primary *trans*-allylic halides reaction takes place between the unrearranged halide and the rearranged secondary form of the Grignard reagent (cf. Young, Roberts, and Wax, *J. Amer. Chem. Soc.*, 1945, **67**, 841). Furthermore it appears that the hydrocarbon forms an azeotrope with 2-ethylbut-3-en-1-ol in order to account for the apparent lower boiling point and their non-separation by distillation.

Requiring stereochemically pure *cis*-hex-3-en-1-ol for further synthetic purposes (cf. Crombie, Harper, Stedman, and Thompson, *J.*, 1951, 2445; Crombie and Harper, *J.*, 1952, 869) and being unable to procure any peppermint oil tailings containing " leaf alcohol " (see Part I), we turned our attention to the selective catalytic hydrogenation of hex-3-yn-1-ol. The course of this semihydrogenation has been the subject of controversy since it was first used by Stoll and Rouvé (*Helv. Chim. Acta*, 1938, **21**, 1542) to synthesise " leaf alcohol." These authors, using colloidal palladium at room temperature, obtained a *cis*-hex-3-en-1-ol that clearly contained *trans*-isomer for the odour differed from that of " leaf alcohol " and the melting point of the 3 : 5-dinitrobenzoate could not be raised above 46°. Takei, Ono, and Sinosaki (*Ber.*, 1940, **73**, 950) found that when using palladised barium sulphate the stereochemical selectivity depended upon the temperature of reduction. At −18° substantially pure *cis*-hex-3-en-1-ol was obtained, giving a pure 3 : 5-dinitrobenzoate (N.B. The configurational symbols used by Takei must be reversed; cf. Part I), whereas at 50° the product gave a mixed 3 : 5-dinitrobenzoate which was separated into the pure *cis*- and impure *trans*-derivative. However, it was not until Sondheimer (*J.*, 1950, 877) devised a one-stage preparation of hex-3-yn-1-ol from acetylene that this route to *cis*-hex-3-en-1-ol became of preparative interest. Nevertheless Sondheimer, using palladised calcium carbonate at room temperature, obtained a *cis*-hex-3-en-1-ol containing a large proportion of *trans*-isomer, as shown by the lack of purity of the 3 : 5-dinitrobenzoate and the quite strong absorption at 10·3 μ indicative of *trans*-isomer

(cf. Part I). It is our general experience that palladised barium sulphate is a more selective catalyst for semihydrogenation of the acetylenic bond than palladised calcium carbonate. In this case too, and in agreement with Takei *et al.*, we find that semihydrogenation of hex-3-yn-1-ol over palladised barium sulphate at 0—20° gives stereochemically pure *cis*-hex-3-en-1-ol, which thus becomes readily accessible. The infrared absorption spectrum was identical with that of natural " leaf alcohol " (cf. Part I) and showed no band at 10·3 μ due to the *trans*-isomer.

To characterise further and to differentiate *cis*- and *trans*-hex-3-en-1-ol we have prepared their *p*-phenylazophenylurethanes. These derivatives differed in colour, crystalline form, and melting point (by 5°), and on admixture gave a large depression of the melting point. The derivative of the *cis*-isomer chromatographed nicely in benzene on alumina and appears suitable for identification of small amounts of " leaf alcohol."

Addition of the Grignard reagent of *cis*-hex-3-enyl bromide to acetic anhydride at −78° (cf. Crombie *et al.*, *loc. cit.*, 1951, " Route E ") gave in good yield *cis*-oct-5-en-2-one (IV) required, *inter alia*, for comparison with the *trans*-isomer (Crombie and Harper, *loc. cit.*, 1952). The absence of a band at 10·3 μ in the infrared absorption spectrum of this ketone showed it to be free from *trans*-isomer. We have characterised *trans*-oct-5-en-2-one further as the semicarbazone. Both the semicarbazone and the 2 : 4-dinitrophenylhydrazone of *cis*-oct-5-en-2-one are anomalous in melting higher than the corresponding derivatives of the *trans*-ketone.



Methoxycarbonylation of *cis*-oct-5-en-2-one gave the keto-ester (V), previously obtained by another route (Crombie *et al.*, *loc. cit.*, 1951), which was converted into *cis*-jasmone (VI) by the last two stages indicated in the reaction scheme. The identity of the product with natural (pure *cis*-)jasmone was established by the identity of the infrared absorption spectra of the ketone and its semicarbazone with those of authentic specimens (Crombie and Harper, *loc. cit.*, 1952), and by the non-depression of melting point on admixture of the semicarbazones and the 2 : 4-dinitrophenylhydrazones. This five-stage route to *cis*-jasmone from " leaf alcohol " (seven stages overall) constitutes the shortest and most practicable synthesis so far devised.

Experimental

The infrared absorption spectra were determined by one of us (R. J. D. S.) with a Grubb-Parsons double-beam spectrometer (rock-salt prism), capillary films of pure liquids or Nujol mulls of solids being used.

trans-*Pent-2-enyl Bromide*.—Pent-1-en-3-ol, prepared on a 4-mole scale by the procedure of Bouis [*Ann. Chim.* (*France*), 1928, **9**, 402], was fractionally distilled through a Dufton column and had b. p. 110—112°/750 mm., n_D^{20} 1·4215 (47% yield). Another preparation, fractionally distilled through a 10-plate column with xylene as a chaser, gave a product of constant b. p. 113·8°/755 mm., n_D^{20} 1·4273. This appears to be an azeotrope of pent-1-en-3-ol with xylene.

Pent-1-en-3-ol was converted, in 0·75-mole portions, into *trans*-pent-2-enyl bromide by the procedure of Part III (Crombie and Harper, *J.*, 1950, 1715) and the product distilled through a Dufton column. The fraction, b. p. 48°/50 mm., n_D^{20} 1·4738 (76% yield), was used. Bouis (*loc. cit.*) gives n_D^{20} 1·4731.

2-*Ethylbut*-3-*en*-1-*ol*.—In accordance with the procedure devised by Gilman and McGlumphy for making allylic Grignard reagents (*Bull. Soc. chim. France*, 1928, **43**, 1322) *trans*-pent-2-enyl bromide (30 g., 0·2 mole) in dry ether (200 ml.) was added during 2 hr. to a stirred suspension of magnesium raspings (10 g., 0·42 g.-atom, sieved to pass 25 mesh) in ether (200 ml.). Paraformaldehyde (12 g., 0·4 mole as formaldehyde) was sublimed in a current of nitrogen during 45 min. into the stirred Grignard reagent, through a wide inlet tube terminating just above the liquid surface. Next day the mixture was treated with saturated ammonium chloride solution (60 ml.) with cooling, and the ether layer decanted and dried (K_2CO_3). After evaporation of

the ether the product was distilled through a short column to give a forerun, b. p. up to 135°, n_D^{20} 1·428, and then 2-ethylbut-3-en-1-ol (11·6 g., 58%), b. p. 135—137°, n_D^{20} 1·430 (Found on different preparations: C, 74·9—75·9; H, 11·8—12·2. Calc. for $C_6H_{12}O$: C, 71·9; H, 12·1%). The residue was distilled to completion from a small flask to give fractions (1·8 g.) within the range of b. p. 140—150°, n_D^{20} 1·431—1·433, none of which resembled " leaf alcohol " in physical properties or odour (" leaf alcohol " has b. p. 154—157°, n_D^{20} 1·4383, see Part I).

In an attempt to purify the crude 2-ethylbut-3-en-1-ol a portion (5·0 g.) and phthalic anhydride (7·4 g.) were heated at 100° in pyridine (4·0 ml.) for 1 hr. The viscous product was dissolved in acetone (20 ml.), and concentrated hydrochloric acid (6 ml.) and ice (6 g.) were added with shaking. On further dilution with ice-water an oil separated which did not crystallise even during several days in a refrigerator. Steam-distillation of the mixture gave an oil which was taken up in ether after saturation of the aqueous phase with potassium carbonate. The ethereal extract was washed with dilute hydrochloric acid and water, dried ($MgSO_4$), and evaporated. Distillation gave fractions (i) b. p. 126—130°, n_D^{20} 1·430 (0·1 g.) (Found: C, 85·4; H, 12·8. Calc. for $C_{10}H_{18}$: C, 86·9; H, 13·1%), considered to be mainly (~90%) hydrocarbon, and (ii) b. p. 135—140°, n_D^{20} 1·433 (0·3 g.), considered to be mainly unchanged 2-ethylbut-3-en-1-ol. Hydrogenation of fraction (i) (14·1 mg.) over palladised barium sulphate led to an absorption of 4·36 ml. (Calc. for 2 double bonds on a mol. wt. of 138: 4·58 ml.), equivalent to 85% decadiene. Renewed steam-distillation after basification with sodium hydroxide gave an oil which was isolated as above and distilled to give *2-ethylbut-3-en-1-ol*, b. p. 137—139°, n_D^{20} 1·4342 (4·0 g.) (Found: C, 71·6; H, 12·0%).

2-Ethylbut-3-enyl 3 : 5-*dinitrobenzoate* crystallised from light petroleum (b. p. 40—60°) as leaflets, m. p. 53° (Found: C, 53·2; H, 4·6. $C_{13}H_{14}O_6N_2$ requires C, 53·05; H, 4·8%), and the 4-*diphenylylurethane* crystallised as fine needles [from light petroleum (b. p. 80—100°)], m. p. 79·5° (Found: C, 77·75; H, 7·2. $C_{19}H_{21}O_2N$ requires C, 77·25; H, 7·2%). In two attempts to prepare the 1-naphthylurethane dehydration ensued and only di-1-naphthylurea was isolated.

2-Ethylbutanol.—Hydrogenation of 2-ethylbut-3-en-1-ol (1·75 g.) in methanol over palladised barium sulphate (5%, 0·3 g.) and distillation of the product gave 2-ethylbutanol, b. p. 144—146°, n_D^{20} 1·421 (1·07 g.). The 3 : 5-dinitrobenzoate crystallised from light petroleum (b. p. 40—60°) as needles, m. p. and mixed m. p. 35°.

trans-3-*Ethylocta*-1 : 5-*diene.*—*trans*-Pent-2-enyl bromide (14·9 g.) in dry ether (10 ml.) was added to magnesium (1·25 g.) under dry ether (25 ml.) as rapidly as the vigour of the reaction permitted. After a further hour's stirring the mixture was worked up as described for 2-ethylbut-3-en-1-ol. Redistilled over sodium, trans-3-*ethylocta*-1 : 5-*diene* (5·8 g., 84%) had b. p. 155—156°, n_D^{20} 1·4322 (Found: C, 86·1; H, 13·2. $C_{10}H_{18}$ requires C, 86·9; H, 13·1%).

cis-*Hex*-3-*en*-1-*ol.*—Hex-3-yn-1-ol was prepared on a 1·75-mole scale in up to 44% yield by Sondheimer's method (*J.*, 1950, 877) and had b. p. 68—69°/15 mm., n_D^{20} 1·453—1·455.

In a typical reduction, hex-3-yn-1-ol (49 g.) was shaken with W-4 Raney nickel in methyl acetate for 20 min. (to remove poisons which otherwise completely inhibited the subsequent hydrogenation; cf. Sondheimer, *loc. cit.*), the solution filtered from the nickel, palladised barium sulphate (5%, 2·0 g.) added, and then reduction effected by shaking in cold water at 15° until 1 mol. of hydrogen had been absorbed. Filtration and distillation then gave *cis*-hex-3-en-1-ol (38·5 g., 79%), b. p. 154—155°, 59·5—61°/14 mm., n_D^{20} 1·4389.

p-Phenylazophenyl *iso*cyanate (200 mg.) (prepared by Raiford and Freyermuth's method, *J. Org. Chem.*, 1943, **8**, 230) and the hex-3-en-1-ol (100 mg.) were refluxed in benzene (10 ml.) for 5 min.; the solution was then concentrated and passed through a column of alumina, elution being with more benzene. Evaporation of the eluate to dryness and crystallisation from acetone–light petroleum (b. p. 40—60°) gave cis-*hex*-3-*enyl* p-*phenylazophenylurethane* as orange leaflets, m. p. 144° (the derivatives of the synthetic and the natural alcohol showed no depression of m. p. on admixture) (Found: C, 66·9; H, 5·8. $C_{19}H_{21}O_2N_3$ requires C, 70·55; H, 6·55%), and trans-*hex*-3-*enyl* p-*phenylazophenylurethane* as red cubes, m. p. 149° (Found: C, 68·0; H, 5·95%). A mixture of the *cis*- and the *trans*-derivative had m. p. 115—120°.

cis-*Oct*-5-*en*-2-*one.*—*cis*-Hex-3-enyl bromide (prepared in 55% yield from the alcohol with phosphorus tribromide at 0°), b. p. 149—151°, n_D^{20} 1·471 [the b. p. 138—140° given by Crombie *et al.* (*J.*, 1951, 2445) appears to be in error], was converted into the Grignard reagent on a 0·1-mole scale and the solution obtained, cooled to −78°, was added during 2 hr. to a stirred mixture of acetic anhydride (100% excess, 0·2 mole) and ether kept at −78°. After a further 2 hours' stirring, the temperature having then reached −10°, saturated aqueous ammonium chloride was added, and the ether layer separated, washed with alkali, dried ($MgSO_4$), and

evaporated. Distillation then gave cis-*oct-5-en-2-one* (65%), b. p. 56—58°/12 mm., n_D^{20} 1·4323 (Found: C, 75·0; H, 11·2. $C_8H_{14}O$ requires C, 76·2; H, 11·2%). The *semicarbazone* crystallised from aqueous ethanol in leaflets, m. p. 114·0—114·5° (Found: C, 58·8; H, 9·0. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·35%), and the 2:4-*dinitrophenylhydrazone* from aqueous ethanol in plates, m. p. 67·5° after chromatography on alumina in benzene (Found: C, 55·4; H, 6·05. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9%).

trans-*Oct-5-en-2-one* [with Dr. F. C. Newman].—Crombie and Harper's ketone (*J.*, 1952, 869) gave a *semicarbazone*, initially separating as an oil and slowly solidifying, which was recrystallised from light petroleum (b. p. 60—80°) and had m. p. 62·5—63·5° (Found: C, 58·9; H, 9·25%). Regenerated from the semicarbazone, *trans*-oct-5-en-2-one had b. p. 59—61·5°/11 mm., n_D^{20} 1·4322. The 2:4-dinitrophenylhydrazone after chromatography on alumina in benzene had m. p. 65·5—66·0°.

Methyl cis-2-*Oxo-oct-5-ene*-1-*carboxylate*.—*cis*-Oct-5-en-2-one (6·3 g., 0·05 mole) in ether was added during 2 hr. to a stirred and refluxed mixture of dimethyl carbonate (9·0 g., 0·1 mole) and sodium hydride (2·4 g., 0·1 mole) in ether and under nitrogen. After being heated and stirred for a further 2 hr. the cooled mixture was poured on glacial acetic acid (10 g.) and ice (10 g.). The ethereal extract was washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and fractionally distilled to give methyl *cis*-2-oxo-oct-5-ene-1-carboxylate (5·2 g., 57%), b. p. 119—122°/9 mm., n_D^{20} 1·4448 (the n_D^{20} 1·4524 given by Crombie *et al.*, *loc. cit.*, appears to be too high).

cis-*Jasmone*.—By Harper's procedure (*J.*, 1946, 892) methyl *cis*-sodio-2-oxo-oct-5-ene-1-carboxylate, prepared with sodium wire or sodium hydride in ether, was treated with bromoacetone, and the crude methyl *cis*-2:5-dioxoundec-8-ene-4-carboxylate so formed was stirred at 70° in 3% aqueous sodium hydroxide to give *cis*-jasmone, isolated by distillation, b. p. 122—124°/9 mm., n_D^{20} 1·4985 (55% yield). The semicarbazone had m. p. and mixed m. p. 204·5—205° and the 2:4-dinitrophenylhydrazone had m. p. and mixed m. p. 118·5—119·0°.

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The Effect of Structure upon Polarographic Behaviour. Part I. The Depolarisation Potentials of Girard-T Compounds.

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The half-wave potentials of the polarographic reduction of the Girard-T compounds of various dialkyl ketones have been measured at 25° in 50% ethyl alcohol buffers at pH 8·0. The results suggest that the electrode process is basically similar to that proposed by Prelog and Häfliger (*Helv. Chim. Acta*, 1949, **32**, 2088). An interpretation of the relative values of $E_{\frac{1}{2}}$ in terms of electronic and steric effects indicates that the branched alkyl groups (Pr^i, Bu^s, and Bu^i) here display steric hindrance, whilst some indication of a similar effect from Pr^n and higher normal groups is found in suitable structures.

Prelog and Häfliger (*Helv. Chim. Acta*, 1949, **32**, 2088) measured the half-wave potentials of the Girard-T derivatives of the C_5–C_{20} cyclanones, demonstrating conformity to the Ilkovic equation and the existence of a two-electron reduction process from the current–potential waves obtained by conventional methods. Moreover, the relative values of these potentials were found to be consistent with the progressive development of a folded ring configuration in the ketones which confers a greater relative stability upon the medium-sized compounds (*ca.* C_9), an effect previously suggested to explain the trend

shown by the ketone cyanohydrin dissociation constants of the same compounds (Prelog and Kobelt, *Helv. Chim. Acta*, 1949, **32**, 1187). Evans and Young (*J.*, 1954, 1310) have shown that the dialkyl ketone cyanohydrin dissociation equilibrium is susceptible to electronic and steric effects from the alkyl groups, and the polarographic reduction of the Girard-T compounds was studied with a similar point in view.

Experimental

Preparation of Ketones.—These were prepared as described by Evans and Young (*loc. cit.*).

Preparation of Girard-T Compounds.—Girard-T reagent (0·3—0·6 mmole) was refluxed for several hours with the ketone (½ mol.) added as a 0·1M-solution. These solutions (1—2 ml. in volume) were contained in glass-stoppered test-tubes and were locally electrically heated. When the stopper was strapped in, the upper part of the tube served as an air condenser for the totally enclosed system and smooth refluxing at 110—130° could be carried out for many hours with no loss of solvent and without the inconvenience of sealing off. After reaction, the solvent was removed under vacuum, leaving a white crystalline solid or a clear syrup. Sufficient ethyl alcohol was added to give a 0·01M-solution of the complex based on the original ketone, together with excess of Girard reagent; 0·5 ml. of this solution was added to 9·5 ml. of previously deoxygenated buffer solution, and hydrogen gas (presaturated with ethyl alcohol) was again passed for a few minutes before a manual polarogram was taken.

The buffer solutions were prepared by mixing two solutions, A (0·08M in each of boric, phosphoric, and acetic acids, and 0·4M in potassium chloride) and B (0·4M in each of potassium chloride and hydroxide), and diluting the mixture with an equal volume of absolute ethyl alcohol. A pH 8·0 buffer is given by 20 ml. of A, 14·5 ml. of B and 34·5 ml. of alcohol, this formulation being essentially that of Britton and Robinson (*J.*, 1931, 1456) with potassium hydroxide instead of sodium hydroxide, 50% ethyl alcohol instead of water, and the addition of 0·2M-potassium chloride in the final solution.

The whole procedure above differs only in minor ways from that used by Prelog and Häfliger (*loc. cit.*) and was adopted for the same reasons. The only important difference is the use of ethyl in place of methyl alcohol.

The standard conditions of polarography were: Temp., 25° (jacketed cell); anode, normal calomel electrode; mercury head, 35 cm. over a 0·01-mm. capillary; drop time, 2·8 sec.; drop weight, 8·24 mg./drop at −1500 mv applied potential.

The potentiometer was calibrated before each measurement against a Doran Potentiometer Type 4246 at 1000 mv, and subsequently recalibrated at every 100 mv in the inflexion range. The currents were measured on a Pye Galvanometer Type 7972 damped by an Ayrton shunt of 1060-ohms resistance, which made the maximum sensitivity 0·0585 μA/scale division.

The results in all cases were obtained from the corrected current–voltage curves given by subtracting the residual current for the buffer from the observed current at each potential. The half-wave potentials, $E_{\frac{1}{2}}$, reported refer in all cases to a complex concentration of $5{\cdot}0 \times 10^{-4}$M, are relative to the normal calomel electrode, and are the means of at least two separate determinations.

The accuracy of these potentials, estimated from the reproducibility in individual cases, is ±10 mv. The values for five measurements on the compound from *n*-hexyl methyl ketone (separate preparations) are given below:

$-E_{\frac{1}{2}}$ (mv)	1488	1490	1487	1501	1511	Mean 1495
i (μA)	2·82	2·82	2·61	2·40	2·40	Mean 2·61

Spectrographic Measurements.—The ultraviolet absorption spectra were determined in absolute ethyl alcohol at room temperature by means of a Unicam S.P. 500 spectrophotometer. The results are given in the Table on p. 1518.

Effect of pH *on the Depolarisation Potentials.*—The variation of the wave form with pH was determined under the standard conditions of polarography for the complexes of *n*-butyl methyl, *tert.*-butyl ethyl, *tert.*-butyl *n*-propyl, di*iso*propyl, and di*iso*butyl ketones. The general observations were: (*a*) At pH's lower than *ca.* 6 the waves become complex, showing two steps. (*b*) The total wave height passed through a maximum at pH 5—7, though the effect was less pronounced for *tert.*-butyl *n*-propyl and di*iso*butyl complexes. (*c*) The waves for di*iso*butyl and *tert.*-butyl *n*-propyl complexes, which are too ill-defined to be measured at pH 8·0, sharpen considerably at lower pH's, but are still relatively ill-defined.

Depolarisation potentials in pH 8·0 *buffer at* 25° (*concn.* 5×10^{-4}M).

Ketone (R·CO·R′)					Ketone (R·CO·R′)				
R	R′ *	$-E_{\frac{1}{2}}$ (v)	i_D (μA)	n	R	R′ *	$-E_{\frac{1}{2}}$ (v)	i_D (μA)	n
Me	Me	1·50	3·10	1·5	Et	Pr^i	1·55	1·64	0·8
Me	Et	1·51	2·81	1·4	Et	Bu^t	1·60	0·76	0·4
Me	Pr^n	1·51	2·75	1·3	Et	C_6H_{11}	1·54	2·34	1·2
Me	Pr^i	1·54	2·22	1·1	Pr^n	Pr^n	1·55	1·57	0·8
Me	Bu^n	1·51	2·98	1·5	Pr^n	Pr^i	1·57	1·05	0·5
Me	Bu^i	1·57	3·10	1·6	Pr^n	Bu^t	No wave at pH 8·0		
Me	Bu^t	1·55	1·29	0·7	Pr^n	C_6H_{11}	1·56	0·82	0·4
Me	*n*-C_6H_{11}	1·51	3·34	1·7	Pr^i	Pr^i	1·55	1·05	0·5
Me	*n*-C_6H_{13}	1·50	2·61	1·3	Pr^i	Bu^t	No wave at any pH		
Me	C_6H_{11}	1·54	2·81	1·5	Pr^i	C_6H_{11}	1·56	0·82	0·4
Et	Et	1·52	2·40	1·2	Bu^i	Bu^i	No wave at pH 8·0		
Et	Pr^n	1·53	2·28	1·1	*cyclo*Hexanone		1·47	3·98	2·0

* C_6H_{11}-*cyclo*Hexyl.

None of these values has been corrected for the *iR* drop over the cell. Prelog and Häfliger found $E_{\frac{1}{2}}$ for *cyclo*hexanone at pH 8·0 to be 1·48 v (corrected from their pH 8·2 value); they also reported alkyl ketones as having $E_{\frac{1}{2}}$ of *ca.* 1·56 v at pH 8·2 with lower i_D's than *cyclo*hexanone.

The graphed results show that $E_{\frac{1}{2}}$ is not a good linear function of pH [d($-E$)/d(pH) decreases as pH increases]. Two approximately parallel plots were obtained for the first and second steps of the di*iso*butyl and *tert.*-butyl *n*-propyl compounds, whilst the points for the single waves of the other compounds (excluding that of di*iso*propyl ketone) lie on the curves for the first step of the double waves. The di*iso*propyl compound is slightly anomalous since its slopes are closer to the theoretical value (0·059 v/pH) than any others, and the point for the single wave at pH 8·0 lies closer to the plot for the second (the more negative) wave, whilst the wave separation is observed as high as pH 7·0. The slopes for the approximate straight lines through these plots are :

			di-Pr^i		Bu^{t}Pr^n		
	Bu^{n}Me	Bu^{t}Et	1st	2nd	1st	2nd	di-Bu^i
$-dE/dpH$ (v/pH) ...	0·10	0·08	0·06	0·06	0·08	0·07	0·08
$-E_{\frac{1}{2}}$ (v) at pH 7 ...	1·44	1·55	1·31	1·55	1·31	1·55	1·31

Analysis of the individual wave profiles by plotting $-E_{applied}$ against $\log i/(i_D - i)$ produced reasonably straight lines with slopes greater than theory for a reversible one-electron process (*viz.*, 0·059 v). There was no marked dependence of slope on pH; the values for the *n*-butyl methyl ketone compound were

pH	5·3	6·0	7·0	8·0	9·0
$-dE_{app.}/d \log i/(i_D - i)$	0·066	0·068	0·064	0·059	0·062

The wave for the *cyclo*hexanone compound at pH 8·0, when similarly treated, gave a value of 0·062 v, which compares with 0·046 v found by Prelog and Häfliger at pH 8·2 in a methyl alcohol solvent. The values of $E_{\frac{1}{2}}$ obtained from these plots were in all cases equal to those found by tangents drawn on the original waves and the latter method was used in all other cases.

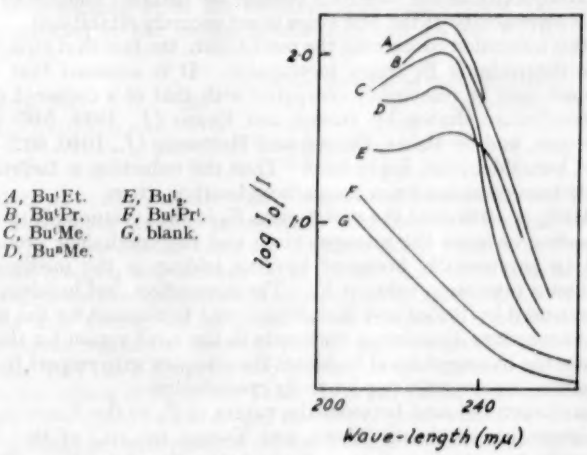
Application of Ilkovic's Equation.—In several instances the dependence of i_D upon the complex concentration at pH 8·0 was demonstrated for small concentration ranges. Ilkovic's equation, $i_D = 605nD^{\frac{1}{2}}cm^{\frac{2}{3}}t^{\frac{1}{6}}_{max.}$, was applied to all waves at pH 8·0, it being assumed that (*a*) that the *cyclo*hexanone compound has a two-electron wave as shown by Prelog and Häfliger, and (*b*) that the *D*'s for all complexes were similarly related to *D* for *cyclo*hexanone *via* their molecular weights. The values of *n* so found are reported in the Table above.

The variability of *n* reflects the variability of i_D since the molecular weights of all the complexes are of a similar magnitude. All the values are less than 2, which agrees with an isolated observation by Prelog and Häfliger concerning alkyl ketones. The results fall into two groups : (*a*) where $n > 1$ and $\simeq 1{\cdot}4$, and (*b*) where $n < 1$ and $\simeq 0{\cdot}6$. It is thought that the lower values of the second group may indicate incomplete complex formation.

Tests for Completeness of Complex Formation.—The failure of the *tert.*-butyl *iso*propyl ketone compound to show a reduction wave at any pH while the waves of *tert.*-butyl *n*-propyl and di*iso*butyl compounds are separated from the background at pH's below 7·0, led to the following tests.

The ketones COBu^{t}Me (12), COBu^{n}Me (8), COBu^{t}Et (22), COBu^{t}Pr^n (22), COBu^{t}Pr^i (36),

and $COBu^i_2$ (16) were subjected to the normal procedure for compound formation, being refluxed for the number of hours shown in parentheses, which were sufficient to give constant diffusion currents in subsequent polarography. The distillates from the vacuum-evaporation were trapped in a solid carbon dioxide–acetone trap and, after suitable dilution with ethyl alcohol, were spectrographically analysed for free ketone. The residues, consisting of compound and excess of Girard-T reagent, were diluted with ethyl alcohol to a concentration of $1{\cdot}25 \times 10^{-4}$M with regard to the Girard compound, complete reaction being assumed, and an ultraviolet spectrum taken. In the Figure these spectra are compared with the spectrum of $3{\cdot}75 \times 10^{-4}$M Girard-T reagent which was unaffected by the refluxing with alcohol. Every ketone except *tert.*-butyl *iso*propyl shows a maximum at 220—230 mμ, which is clearly due to the compound. In every case except from *tert.*-butyl methyl and *n*-butyl methyl traces of ketone were present in the distillates. It is concluded that *tert.*-butyl *iso*propyl ketone does not



form a compound under the conditions used, whilst the formation may be incomplete, owing to attainment of an equilibrium, in $COBu^tEt$, $COBu^tPr^n$, and $COBu^i_2$.

These results make the reliability of the n values in the above Table doubtful, especially when n is very low ($<0{\cdot}5$). On the other hand, the failure to achieve a Girard compound concentration of 5×10^{-4}M would have no appreciable effect on $E_{\frac{1}{2}}$.

Discussion

The above results present the same general pattern as those of Prelog and Häfliger (*loc. cit.*), *viz.*, the existence of a maximum i_D at *ca.* pH 7·0, the appearance of two steps in waves at pH's below 6·0, and the large slope of the $E_{\frac{1}{2}}$–pH plots are common to both the series of compounds. However, the detail in the alkyl ketone compounds shows a greater variation of type and the departure from the reversible behaviour is wider.

Prelog and Häfliger proposed the following mechanism for the electrode-reduction process by analogy with the mechanism of polarographic ketone reduction (see Kolthoff and Lingane, " Polarography," Interscience Publ., 1952, Vol. II, p. 663, 683) :

$$\begin{array}{l} \overset{N}{\underset{CR_1R_2}{}}\text{·NH·CO·CH}_2\text{·}\overset{+}{\text{N}}\text{Me}_3 + \text{H}^+ \underset{-e}{\overset{+e}{\rightleftharpoons}} \overset{NH\text{·NH·CO·CH}_2\text{·}\overset{+}{\text{N}}\text{Me}_3}{\underset{\cdot CR_1R_2 \qquad \text{(I)}}{}} \\ \text{(I)} + \text{H}^+ + e \longrightarrow \overset{NH\text{·NH·CO·CH}_2\text{·}\overset{+}{\text{N}}\text{Me}_3}{\underset{CHR_1R_2}{}} \end{array}$$

They supported this choice by isolating the dimer of the radical (I) in preparative experiments. The departures from truly reversible behaviour were ascribed to the irreversibility of the second step.

Berzins and Delahay (*J. Amer. Chem. Soc.*, 1953, **75**, 5716), in a theoretical treatment of

an identical mechanism, find that both the wave profile and the value of $E_{\frac{1}{2}}$ at constant pH depend upon the rate of the irreversible step. Their results, when applied to the present process, suggest that $E_{\frac{1}{2}}$ should vary more rapidly with pH than 0·059 v/pH, as found, but the waves should tend to become single as the pH decreases, in contradiction to the observed changes.

The variation of i_D with pH, which is a feature of the aldehyde and ketone reductions also, and the observation that the double waves of the acid region have sections of approximately equal heights, are not easily explained and invite comparison with the reduction of formaldehyde and acetaldehyde (Vesseley and Brdicka, *Coll. Czech. Chem. Comm.*, 1947, **12**, 307; Bieber and Trumpler, *Helv. Chim. Acta*, 1947, **30**, 706, 1109, 2000), and of glyoxal (Elving and Bennett, *J. Amer. Chem. Soc.*, 1954, **76**, 1412). This survey emphasises the complexity of the electrode process for Girard-T compound reduction and suggests that the reversibility of the first stage is not securely established.

Apart from this indecision concerning the mechanism, the fact that structural influences are operative in determining $E_{\frac{1}{2}}$ seems inescapable. It is assumed that reduction of a Girard-T compound may be reasonably compared with that of a carbonyl compound, and therefore, the conclusions drawn by Davies and Evans (*J.*, 1939, 546) concerning the alkyl phenyl ketones, and by Baker, Davies, and Hemming (*J.*, 1940, 692) concerning the *para*-substituted benzaldehydes, apply here. Thus the reduction is facilitated, and $E_{\frac{1}{2}}$ is decreased, by electron recession from the carbonyl-carbon atom.

Prelog and Häfliger attributed the variation in $E_{\frac{1}{2}}$ in the cyclanone Girard-T compounds to hydrogen bonding between the nitrogen atom and ring-methylene groups. The effect was considered to be sterically favoured by ring folding in the medium-sized ketones (C_8–C_9) which show a maximum value of $E_{\frac{1}{2}}$. The same effect, but involving the carbonyl-oxygen atom, was used by Prelog and Kobelt (*loc. cit.*) to account for the maximum value shown by the cyanohydrin dissociation constants in the same region for the same ketones. In the former case the hydrogen bond stabilises the complex with respect to the radical (I); in the latter, the free ketone with respect to its cyanohydrin.

A similar parallelism is found between the values of $E_{\frac{1}{2}}$ in the Table (p. 1518) and the cyanohydrin dissociation constants (Evans and Young, *loc. cit.*) of the dialkyl ketones. Thus it is roughly true to say that $-E_{\frac{1}{2}}$ is proportional to $K_{35°}$—the cyanohydrin dissociation constant. There is, however, an important quantitative difference between the two series of compounds, as comparable changes of $E_{\frac{1}{2}}$ are accompanied by much larger changes of the dissociation constants in the cyclanone series, *e.g.*:

	Cyclanone			Ketone	
Compound	C_6	C_9	Compound	$COMe_2$	$COBu^tEt$
$-E_{\frac{1}{2}}$ (v) at 20°	1·51	1·63	$-E_{\frac{1}{2}}$ (v) at 25°	1·50	1·60
10^2K_{20}	0·1	170·0	10^2K_{20}	2·9	7·3
$\Delta G°_{\text{Diss.}}$ (kcal.)	4·2	−0·3	$\Delta G°_{\text{Diss.}}$ (kcal.)	2·1	1·6

This contrast suggests that there is a difference in kind between the effects operating in the two series.

When the same quantities for the *para*-substituted benzaldehydes, and for acetaldehyde and acetone, are compared, it is found that larger changes of $E_{\frac{1}{2}}$ are linked with smaller changes of K than occur in the alkyl ketones and their Girard-T compounds.

	Benzaldehyde			
Compound	*p*-Cl	*p*-OMe	CH_3·CHO	$COMe_2$
$-E_D$ (v)	1·05 [a]	1·22 [a]	1·87 [b]	2·10 [c]
10^2K_{20}	0·49 [d]	3·1 [d]	0·76 [e]	2·9
$\Delta G°_{\text{Diss.}}$ (kcal.)	3·0	2·0	2·9	2·1

The conditions under which the above E_D's were measured were not identical but this should not invalidate the comparisons. (*a*) Baker, Davies, and Hemming (*loc. cit.*); (*b*) Adkins and Cox (*J. Amer. Chem. Soc.*, 1938, **60**, 1151); (*c*) Stackelburg and Stracke (*Z. Elektrochem.*, 1949, **53**, 118); (*d*) Lapworth and Manske (*J.*, 1928, 2533); (*e*) Jones (*J.*, 1914, **105**, 1506).

It is believed that the simultaneous increases of $-E_D$ and K reported for these compounds are due to the relative degrees of electron release (cf. Baker, Davies, and Hemming, *loc. cit.*), steric effects being absent.

The depolarisation potentials of the Girard-T compounds of the dialkyl ketones are regarded as being controlled by similar electronic (inductive and hyperconjugative) and steric effects to those postulated as determining the extent of the cyanohydrin dissociations for the same compounds (Evans and Young, *loc. cit.*). The magnitude of the electron-release effect is indicated by the sequence of $-E_{\frac{1}{2}}$ for the *n*-alkyl methyl compounds, all of which fall within the range **1·50—1·51** v. Comparison of pairs of compounds containing the normal and branched isomeric groups together with a common group, shows the branched molecule to have an $E_{\frac{1}{2}}$ value **0·03—0·04** v more negative than the normal one. On the basis of electron-release effects alone, the compound containing the normal group would be expected to have the more negative value owing to its potentially higher hyperconjugation effect.

The effects of branching upon the electrode-reduction process and the cyanohydrin equilibrium are revealed by the sequences of $-\Delta E_{\frac{1}{2}}$ and ΔK for ($CORPr^{i}$ — $CORPr^{n}$) as *R* becomes larger, *e.g.* :

	Common group R in the compound :				
$\Delta(Pr^{i}–Pr^{n})$	Me	Et	Pr^{n}	*cyclo*-C_6H_{11}	Pr^{i}
$-\Delta E_{\frac{1}{2}}$ (v)	0·03	0·02	0·03	0	−0·03
$10^{3}\Delta K_{25}$	−3·7	−3·8	−2·5	−0·9	+8·4
$\Delta(\Delta G^{\circ})$ (kcal.)	0·3	0·3	0·2	0·1	−0·4

The positive values of $-\Delta E_{\frac{1}{2}}$ indicate that the *branched* isomers are the more difficult to reduce, whilst the common group is *unbranched*. On the other hand the negative values of ΔK show that the *unbranched* ketones are the more stable relative to their cyanohydrins whilst the common group is *unbranched*. It is thought that these situations arise because the cyanohydrin dissociation equilibrium is only markedly susceptible to the steric meshing effect (see Evans and Young, *loc. cit.*) and is electronically controlled throughout the normal group sequence, whilst the electrode process suffers a greater steric impedance from the *iso*propyl than from the *n*-propyl group as long as the common group is smaller than *n*-propyl. Thus the values of $E_{\frac{1}{2}}$ in the Table on p. 1518 show that the decreasing ease of reduction of complexes based on the *n*- and *iso*-propyl groups is di-Pr^{n} = di-Pr^{i} > $Pr^{i}Pr^{n}$. It therefore seems that the extra electron release from di-Pr^{n} is equivalent to the additional steric effect in di-Pr^{i}, while $Pr^{i}Pr^{n}$ has a steric impedance comparable with that of di-Pr^{i} with a larger electron release. This conclusion is supported by the pattern of the other results and also by the close similarity of the behaviours of the *cyclo*hexyl and the *iso*propyl group. The alternative to this steric explanation of the results would require anomalous variations among the alkyl-group inductive effects; *e.g.*, EtMe −1·51, EtEt −1·52 v, but Bu^{t}Me −1·55, Bu^{s}Et −1·60 v.

The differences observed among the alkyl phenyl ketones are consistent with this hypothesis, *e.g.*,

$-\Delta E_{D}$ ($Pr^{i}–Pr^{n}$)	0·03 v	(pH ≏7) (Davies and Evans, *loc. cit.*)
$10^{3}\Delta K_{20}$	−65	(Lapworth and Manske, *J.*, 1930, 1976)

where the hyperconjugation of the *n*-propyl group is enhanced by the phenyl nucleus. The failure of the *para*-alkylbenzaldehydes to show the effect is also expected, as no alkyl-group steric effects are present (Baker, Davies, and Hemming, *loc. cit.*; Baker and Hemming, *J.*, 1942, 191). In a similar way the depolarisation potentials of the aliphatic aldehydes (Adkins and Cox, *J. Amer. Chem. Soc.*, 1938, **60**, 1151) are free from any branched-group effect since the alkyl groups are accompanied by the small hydrogen atom on the carbonyl carbon atom.

A greater susceptibility of the cathodic compound reduction to steric influence than is observed in a kinetic equilibrium involving similar structures might be caused by orientation of the compound at the electrode surface. Thus attachment of the quaternary grouping to the mercury surface would leave the variable alkyl groups protecting approaches from the solution side. In this situation attachment of a proton to the doubly-bonded nitrogen atom might meet a higher energy barrier when the alkyl groups are branched. A comparable case of steric impedance has been postulated by Leonard, Laitinen, and Mottus (*J. Amer. Chem. Soc.*, 1953, **75**, 330) to explain $E_{\frac{1}{2}}$ differences, of similar magnitude

to the present ones, which occur during the reduction of alkane-1 : 2-diones at the dropping-mercury electrode. The standard oxidation potentials of the alkyl ketones determined by Adkins, Elofson, Rossow, and Robinson (*ibid.*, 1949, **71**, 3622) and by Day, Robinson, Bellis, and Till (*ibid.*, 1950, **72**, 1379) are free from any consistent structural effects of the type described above. This may be due to the fact that a kinetic equilibrium process was used for their measurement.

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Tracer Studies on Ester Hydrolysis. Part II. The Acid Hydrolysis of* tert.*-Butyl Acetate.*

By C. A. Bunton and J. L. Wood.

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Isotopic tracer studies on the acid-catalysed hydrolysis of *tert.*-butyl acetate, in water and in aqueous dioxan, show that although the fission in water is predominantly of the alkyl–oxygen bond ($A_{Al}1$), yet in aqueous dioxan it is largely of the acyl–oxygen bond. Kinetic studies show a marked increase in hydrolysis rate in going from aqueous dioxan to pure water, and this increase in rate can be correlated with the change of position of bond fission.

Carboxylic esters of tertiary aliphatic alcohols provide a favourable system for the observation of alkyl–oxygen fission in hydrolysis. The observation of racemisation with accompanying inversion of the alcohol obtained in the acid hydrolysis of optically active ethylmethyl*iso*hexylcarbinyl (1-ethyl-1 : 5-dimethylhexyl) acetate (Bunton, Hughes, Ingold, and Meigh, *Nature*, 1950, **166**, 679) demonstrates the existence of this bond fission. Similarly, the products isolated show that methanolysis of some *tert.*-butyl esters involves alkyl–oxygen bond fission (Cohen and Schneider, *J. Amer. Chem. Soc.*, 1941, **63**, 3382). In these systems hydrolysis or methanolysis in the presence of alkali gives acyl–oxygen bond fission.

The comparable system of the acid hydrolysis of *tert.*-butyl acetate has been studied by the use of ^{18}O as an isotopic tracer. In this system the aqueous hydrolysis was shown to involve fission of the alkyl–oxygen bond (Bunton, Comyns, and Wood, *Research*, 1951, **4**, 383). However, owing to the low solubility of the ester in water the hydrolysis was carried out under heterogeneous conditions, and it is convenient therefore to supplement the evidence obtained in hydrolysis by water with that of homogeneous acid hydrolysis in aqueous dioxan.

The observation of minima in the value of the acid catalysis constant throughout a series of esters (acetates and succinates), in which the alkyl group is varied from methyl to ethyl, *iso*propyl, and *tert.*-butyl (Olsson, *Z. phys. Chem.*, 1928, **133**, 233; Skrabal and Hugetz, *Monatsh.*, 1926, **47**, 17; Meyer, *Z. phys. Chem.*, 1909, **66**, 96; Homan, *Rec. Trav. chim.*, 1944, **63**, 181), can be interpreted as a possible change of mechanism from $A_{Ac}2$ to $A_{Al}1$. However, the existence of a pre-equilibrium between the neutral ester molecule and its conjugate acid precludes the use of this evidence as an unambiguous test for a change of mechanism, particularly as an increase in the inductive electron release from the alkyl group will favour the conjugate acid.

Position of Bond Fission.—The position of bond fission in ester hydrolysis can be determined unambiguously by the use of ^{18}O as an isotopic tracer, provided always that the possibility of extraneous isotopic exchange is eliminated by blank tests. In the experiments described here the *tert.*-butyl alcohol was isolated from the reaction mixture by direct distillation or by azeotropic distillation with benzene. The oxygen isotopic content of the *tert.*-butyl alcohol was determined by various methods; in certain experiments the alcohol–benzene azeotrope was pyrolysed over platinised quartz, and the oxides of carbon so produced were reduced by hydrogen to water with a thoriated nickel catalyst, the general

* Part I, *J.*, 1955, 1354.

method devised for elementary analysis of oxygen (Russell and Fulton, *Ind. Eng. Chem. Anal.*, 1933, **5**, 384). The water produced was then equilibrated with carbon dioxide. This general method has certain disadvantages: the large surfaces increase adsorption, and dilution and memory effects are large; therefore considerable time has to elapse between samples, and large samples (*ca.* 2 g.) of the alcohol are desirable.

In later experiments the sample was pyrolysed *in vacuo* over Monel gauze at 850°, or in a carbon tube heated *in vacuo* to *ca.* 1200° in an induction furnace. The latter methods give carbon monoxide directly, and the isotopic analyses were carried out directly on this gas.

The isotopic results and the methods used are listed in Table 1. This shows that acid

TABLE 1. *Hydrolyses in isotopically enriched solvents at 25°.*

Expt. no.	Solvent	[H⁺]	Time (hr.)	^{18}O abundance (atoms % excess) H_2O	^{18}O abundance (atoms % excess) Bu^tOH	Alkyl–oxygen fission (%)
1	Water	0·24	48	0·522	0·506	97
2	,,	0·175	26	0·438	0·428 *	98
3	Aq. 70% dioxan	0·175	144	0·438	0·153 *	35
4	,, ,,	0·240	70	0·438	0·165 *	38
Blank tests:						
	Water	0·27	48	0·327	0·026	
	Aq. 70% dioxan	0·17	98	0·692	0·011	
	,, ,,	0·167	98	0·692	0·010	

* Isotopic analyses by direct pyrolysis to CO.

hydrolysis in water gives almost complete alkyl–oxygen bond fission; in aqueous dioxan this proportion is reduced to *ca.* 36%. In neither solvent does the exchange of the alcohol complicate the result. The significance of these results can only be considered with the dependence of acid hydrolysis rate on the water content of the solvent.

Kinetics of Acid Hydrolysis.—The kinetics of acid hydrolysis of *tert.*-butyl acetate were followed by acid–alkali titration (Table 2). The effect of an increase in the water content is to increase the overall rate of hydrolysis and to modify the mechanism. If we assume that the isotopic evidence for alkyl–oxygen bond fission, obtained under non-kinetic conditions in water, can be applied to the more dilute solutions used in the rate measurements, the rates of acyl and alkyl oxygen bond fission can be calculated for the two solvents used (Table 3).

TABLE 2. *Kinetics of acid hydrolysis of* tert.*-butyl acetate at 25°.*

[H⁺] (mole l.⁻¹)	[CNS⁻]	10^7k_1 (sec.⁻¹)	10^6k_A (sec.⁻¹ mole⁻¹ l.)	[H⁺] (mole l⁻¹.)	[CNS⁻]	10^7k_1 (sec.⁻¹)	10^6k_A (sec.⁻¹ mole⁻¹ l.)
Solvent: H_2O				*Solvent*: Aq. 70% dioxan			
0·0996	0·109	141	142 *	0·0984	—	6·72	6·82
0·0996	0·170	148	149 *	0·0984	—	6·60	6·70

* These values are comparable with those obtained by Skrabal (*loc. cit.*), *viz.*, $1·26 \times 10^{-4}$ sec.⁻¹ mole⁻¹ l.; the difference is presumably due to the greater ionic strength of the solutions used in this work. Extrapolation to the ionic strength of Skrabal's work gives $k_A = 1·28 \times 10^{-4}$ sec.⁻¹ mole⁻¹ l.

TABLE 3. *Rates of acid-catalysed alkyl- and acyl–oxygen fissions at 25°.**

Solvent	10^6k_A (overall)	10^6k_A (alkyl)	10^6k_A (acyl)
H_2O	128	*ca.* 124	*ca.* 4
Aq. 70% dioxan	6·76	2·4	4·3

* The percentages of alkyl–oxygen fission are taken as 97 and 36 in water and aqueous dioxan, respectively: the enrichment due to exchange between the alcohol and water is ignored.

This analysis shows that, whereas the rate of acid-catalysed acyl–oxygen fission ($A_{Ac}2$) is almost independent of the water content of the solvent (cf. hydrolysis of ethyl acetate by the $A_{Ac}2$ mechanism; Lapworth, *J.*, 1908, **93**, 100; Burrows, *J.*, 1919, **115**, 1230), the corresponding alkyl–oxygen fission is accelerated by an increase in the water content of the solvent. This solvent effect on the $A_{Al}1$ mechanism in *tert.*-butyl acetate is qualitatively similar to that observed in the acid hydrolysis of triphenylmethyl acetate (Part I), and in the

acid hydrolysis of di-*tert.*-butyl succinate (Homan, *loc. cit.*), where we assume the positions of bond fission to be qualitatively similar to those observed in this work.

The overall mechanism of acid hydrolysis of *tert.*-butyl acetate in water by $A_{Al}1$ can be formulated as

$$CH_3{\cdot}CO_2{\cdot}CMe_3 + H^+ \overset{\text{Fast}}{\rightleftharpoons} [CH_3{\cdot}CO_2H{\cdot}CMe_3]^+$$

$$[CH_3{\cdot}CO_2H{-}{-}CMe_3]^+ \overset{\text{Slow}}{\rightleftharpoons} CH_3{\cdot}CO_2H + {}^+CMe_3$$

$${}^+CMe_3 + H_2O \overset{\text{Fast}}{\rightleftharpoons} CMe_3{\cdot}OH + H^+$$

The mechanism $A_{Al}1$ involves a carbon–oxygen heterolysis as the rate-determining step of the reaction. Such heterolyses frequently generate a carbonium ion of sufficiently long life for it to be captured by a reagent other than the water molecule. Such intervention experiments have frequently been made with sodium azide as the reagent (*e.g.*, Bateman, Hughes, and Ingold, *J.*, **1940**, 974). It was thought possible that, in the acidic solutions used in these ester hydrolyses, the thiocyanate ion would be a more useful intervening agent. The hydrolysis of diphenylmethyl chloride in aqueous dioxan was in fact subject to marked intervention by this reagent. However, in water both the acid hydrolysis of *tert.*-butyl acetate and the hydrolysis of *tert.*-butyl chloride show no such intervention by thiocyanate, and this test therefore gives no evidence on the precise nature of the alkyl–oxygen fission examined.

Experimental

Preparation of Materials.—*tert.*-Butyl acetate was prepared from the alcohol by treatment with acetyl chloride in the presence of pyridine (Abramovitch, Shivers, Hudson, and Hauser, *J. Amer. Chem. Soc.*, **1943**, **65**, 986). A typical specimen had b. p. 97—98°, n_D^{25} 1·3480 (Found: C, 62·7; H, 10·5. Calc. for $C_6H_{12}O_2$: C, 62·2; H, 10·4%). Dioxan was purified by decomposition of the acetals with hydrochloric acid in a stream of nitrogen, followed by washing, drying, and finally distillation over sodium. The aqueous 70% dioxan solvent was made up by volume at room temperature.

Kinetic Measurements.—The kinetic runs were made in stoppered flasks. Samples were withdrawn at suitable intervals, the reaction stopped by addition of acetone, and the acid titrated with standard barium hydroxide. The rate coefficients were calculated from the equation $k_1 = [2{\cdot}3/(t_2 - t_1)]\log_{10}(a - x_1)/(a - x_2)$, where $(a - x_1)$ and $(a - x_2)$ are the concentrations of ester at times t_1 and t_2, respectively, and t is in seconds.

The possibility of intervention by thiocyanate ion in the hydrolyses of both *tert.*-butyl acetate and *tert.*-butyl chloride was tested by estimation of inorganic thiocyanate, in the course of the kinetic run, with silver nitrate. No intervention was observed in any of these hydrolyses. A typical experiment illustrating the kinetic form of hydrolyses and the non-intervention of thiocyanate ions is quoted below:

Run 33. Temp. 25·00° ± 0·05°. [HCl] = 0·0996M, [Bu^tOAc] = 0·0539M, [KCNS] = 0·170M. Solvent, water.

Acid estimation: 2·90-c.c. samples were titrated with 0·0599N-barium hydroxide. Thiocyanate estimation: 2·90-c.c. samples were back-titrated with 0·0452M-thiocyanate after addition of 10 c.c. of 0·1013N-silver nitrate.

Time (min.)	Acid titre (c.c.)	10^5k_1 (sec.$^{-1}$)	CNS^- titre (c.c.)	Time (min.)	Acid titre (c.c.)	10^5k_1 (sec.$^{-1}$)	CNS^- titre (c.c.)
0	5·00	—	—	1197	6·54	1·35	4·57
46	—	—	4·50	1585	6·77	1·40	—
136	5·36	1·48	4·65	7 days	7·35, 7·37	—	—
261	5·59	1·62	4·65	α (calc.)	7·42	—	—
396	5·80	1·54	4·60				

Mean value of $k_1 = 1{\cdot}48 \times 10^{-5}$ sec.$^{-1}$; $k_A = 1{\cdot}49 \times 10^{-4}$ sec.$^{-1}$ mole^{-1} l.

Position of bond fission. To minimise extraneous exchange between the *tert.*-butyl alcohol and water the hydrolyses were stopped after *ca.* 40% reaction.

The alcohol was isolated from the aqueous dioxan solvent by the following procedure. The solution was saturated with sodium sulphate and extracted with ether, and, after drying (K_2CO_3), the ether was evaporated. It was found that the alcohol could be separated as its azeotrope with benzene (Young, *J.*, **1902**, **81**, 746), with no contamination by dioxan or *tert.*-butyl acetate.

This isolation in the benzene azeotrope was used in one of the hydrolyses in water (Expt. 1). In the other (Expt. 2), the unhydrolysed ester was extracted with chloroform, the acid first neutralised, and the alcohol isolated by fractional distillation. Blank tests were carried out under the general conditions of the hydrolyses.

Expt. 2. Hydrolysis in water. The ester (5 c.c.) was shaken in 100 c.c. of enriched water ($[HClO_4]$ = 0·175M) for 26 hr. at 25°. The unchanged ester was extracted with chloroform, and the *tert.*-butyl alcohol distilled from a low-hold-up, metal spiral-packed column (b. p. 82·5—82·8°, n_D^{25} 1·3850).

Expt. 3. Hydrolysis in aqueous dioxan. The ester (10 c.c.) was hydrolysed in 100 c.c. of solvent for 144 hr. at 25°. The crude ether extract was dried, the ether evaporated, dry benzene added, and the azeotrope (b. p. 73·0—73·4°, n_D^{25} 1·4495) obtained by fractionation.

Two general methods were used for the isotopic assays. In the first (used for the product of Expt. 1), the alcohol was pyrolysed over hot platinised quartz, and the carbon oxides reduced with hydrogen over a thoriated nickel catalyst by the general method of Russell and Fulton (*loc. cit.*). The water produced was equilibriated with carbon dioxide, and this gas analyzed mass-spectrometically.

This method required comparatively large samples and was subject to large dilution and memory effects, and direct pyrolysis to carbon monoxide was used for most of the experiments. The samples of carbon monoxide were analyzed mass-spectrometrically; the absence of atmospheric nitrogen (giving mass 28) was demonstrated by the absence of argon.

The authors are indebted to Dr. A. E. Comyns for assistance with the experiments on the exchange of *tert.*-butyl alcohol, to Mr. T. A. Lewis for carrying out many of the pyrolyses, and to Dr. D. R. Llewellyn for a supply of $H_2^{18}O$. They are most grateful to Professors E. D. Hughes, F.R.S., and C. K. Ingold, F.R.S., for their advice.

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The Oxidation of Olefins with Perbenzoic Acids. A Kinetic Study.

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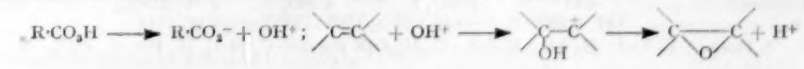
The rates of epoxidation of various olefins with substituted perbenzoic acids have been measured at four temperatures, and the entropies, free energies, and heats of activation have been calculated. A theory is advanced for the mechanism of the reaction.

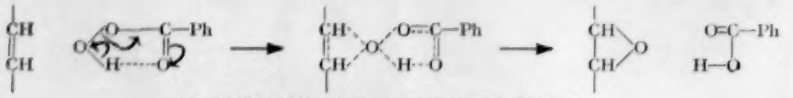
PER-ACID oxidation of olefins in non-polar solvents gives excellent yields of the corresponding epoxides (cf. Swern, "Organic Reactions," Wiley, 1953, Vol. VII, p. 378), and has been shown (cf. Boeseken and Blumberger, *Rec. Trav. chim.*, 1925, **44**, 90; Boeseken and Stuurman, *ibid.*, 1937, **56**, 1034; Medvedev and Blokh, *J. Phys. Chem. U.S.S.R.*, 1933, **4**, 721) to be of the first order with respect to both olefin and per-acid. Since the relative reaction velocities of various olefins indicate that the per-acids are electrophilic reagents (Swern, *J. Amer. Chem. Soc.*, 1947, **69**, 1692), it has been suggested that the per-acids act by the provision of free hydroxyl cations (Robertson and Waters, *J.*, 1948, 1574; Weisenborn and Taub, *J. Amer. Chem. Soc.*, 1952, **74**, 1329), *i.e.*:



However, epoxidation always results in *cis*-addition (see, *e.g.*, Braun, *ibid.*, 1929, **51**, 228; Witnauer and Swern, *ibid.*, 1950, **72**, 3364; King, *J.*, 1942, 387; Atherton and Hilditch, *J.*, 1943, 204), thus precluding formation of a free carbonium ion (unless the life of the ion is less than the period of rotation about a single bond). Waters (Gilman, "Organic Chemistry," Wiley, New York, 1953, Vol. IV, p. 1165) has stated that, since epoxidation is a bimolecular process, the hydroxyl cation cannot become a free entity, and has proposed a modified mechanism which is analogous to that of the addition of halogens to olefins.

Swern (*op. cit.*, p. **386**) has suggested a mechanism involving acid-catalysis, giving a transition state which is reminiscent of that for the acid-catalysed fission of epoxides (cf. Hammett, " Physical Organic Chemistry," McGraw-Hill, 1940, Chapter VI).

The present paper reports the rates of epoxidation of various olefins by substituted perbenzoic acids in benzene and diethyl ether solutions, with the object of extending to epoxidation the molecular mechanisms recently proposed for the mode of action of perbenzoic acid on substituted benzaldehyde phenylhydrazones (Lynch and Pausacker, *J.*, 1954, **1131**), 4 : 4′-dichlorodibenzyl sulphide (Overberger and Cummins, *J. Amer. Chem. Soc.*, 1953, **75**, 4250), and diphenyl sulphoxide (Szmant, Harnsberger, and Krahe, *ibid.*, 1954, **76**, 2185), *i.e.* :



(Cf. Bartlett, *Record Chem. Progr.*, 1950, **11**, 51.)

Experimental

M. p.s are corrected. " Peroxide " oxygen was determined by iodometric titration (see below). Other analyses were performed under the direction of Dr. K. W. Zimmermann.

Reagents.—Substituted perbenzoic acids were prepared by Braun's method (*Org. Synth.*, Coll. Vol. I, 1946, p. 431) as modified by Kolthoff, Lee, and Mairs (*J. Polymer Sci.*, 1947, **2**, 199) and Overberger and Cummins (*loc. cit.*). M. p.s, yields, and analyses are given in the following Table. M. p.s in parentheses are those reported in the literature.

Substituent	M. p.	Yield (%)	" Peroxide " oxygen Found (%)	" Peroxide " oxygen Required (%)
4-OMe	86° (86°)	60	9·2	9·5
4-Me	95 (95)	93	10·4	10·5
Nil	40 (41)	94	10·9	11·6
4-Cl	108 (111)	32	9·3	9·3
3-Cl	88	66	9·4	9·3
3-NO_2	101	66	8·5	8·7
4-NO_2	136 (134)	42	8·7	8·7

Diethyl ether was purified by Vogel's method (" A Textbook of Practical Organic Chemistry," Longmans, 1950, p. 162).

Benzene was purified by Vogel's method (*op. cit.*, p. 171) and dried over sodium.

Magnesium perchlorate (B.D.H. " Anhydrous ") was dried at 110° for 4 hr. immediately before use.

Benzoic acid was recrystallised from ethanol and had m. p. 122°.

Monosubstituted *trans*-stilbenes were prepared by the Meerwein reaction (cf. Meerwein, Buchner, and Emster, *J. pr. Chem.*, 1939, **152**, 237). *trans*-4 : 4′-Dimethoxystilbene was obtained by reduction of *p*-anisaldehyde with alkaline ethylene glycol (Tadros, Ekladius, and Sakla, *J.*, 1954, 2351). The *trans*-stilbenes were crystallised from ethanol immediately before use. Their m. p.s are given in the following Table.

Substituent	4-OMe	3-Me	4-Me	Nil	3-Cl
M. p.	134° (135°)	52° (53°)	118° (117°)	123° (123°)	73° (73°)
Substituent	4-Cl	3-NO_2 *	4-NO_2	4 : 4′-$(OMe)_2$	
M. p.	130° (129°)	113°	157° (155°)	214° (214°)	

* Found : C, 75·1; H, 4·9; N, 6·2. $C_{14}H_{11}O_3N$ requires C, 74·7; H, 4·9; N, 6·2%.

Styrene was twice distilled immediately before use (b. p. 146°).

cis-Stilbene, b. p. 140°/10 mm., was prepared by Taylor and Crawford's method (*J.*, 1934, 1130).

Triphenylethylene was prepared by Adkins and Zartman's procedure (*Org. Synth.*, 1937, **17**, 89) and after crystallisation from ethanol had m. p. 71° (lit., 72°).

Tetraphenylethylene, m. p. 224° (lit., 223—224°) was prepared by reduction from benzophenone *via* benzpinacol and benzpinacolone (cf. Bachmann, *J. Amer. Chem. Soc.*, 1934, **56**, 449), and was crystallised from benzene–ethanol.

*cyclo*Hexene, b. p. 83°, was purified by Waterman and van Westen's method (*Rec. Trav. chim.*, 1929, **48**, 637).

Apparatus.—A bath was used whose temperature was controlled to within ±0·05°. Reactions were performed in calibrated standard 50-ml. flasks. Blackened flasks were used for the reactions with *cis*-stilbene.

Yields of Products.—The appropriate olefin (*ca.* 2·5 × 10^{-3} mole) was added to a solution of perbenzoic acid (*ca.* 2·8 × 10^{-3} mole) in benzene (100 ml.), and the mixture was kept at 30° for 4 days. Residual acids were removed by extraction with sodium hydrogen carbonate, and the solvent was evaporated under reduced pressure. The residues were purified by crystallisation (from ethanol) or distillation. Yields, etc., of the epoxides are listed in the Tables.

(a) trans-*Stilbene epoxides.*

Substituent	4 : 4′-$(OMe)_2$	4-OMe	4-Me	3-Me [a]	Nil
M. p.	142° (142°)	119° (118°)	61° (59°)	66°	68° (69°)
Yield (%)	98	95	99	99	100
Substituent	3-Cl [b]	4-Cl [c]	3-NO_2 [d]	4-NO_2	
M. p.	60°	100°	81°	125° (125°)	
Yield (%)	95	96	98	96	

[a] Found: C, 85·8; H, 7·0. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%. [b] Found: C, 72·6; H, 5·3; Cl, 15·3. $C_{14}H_{11}OCl$ requires C, 72·9; H, 4·8; Cl, 15·4%. [c] Found: C, 72·8; H, 4·6; Cl, 15·2%. [d] Found: C, 69·4; H, 4·5; N, 6·2. $C_{14}H_{11}O_3N$ requires C, 69·7; H, 4·6; N, 5·8%.

(b) *Other epoxides.*

Epoxide	Styrene	*cis*-Stilbene	$CHPh:CPh_2$	$CPh_2:CPh_2$	*cyclo*Hexene
M. p./B. p.*	101°/40 mm.*	43° (42°)	78° (75—77°)	200° (201°)	132° *
Yield (%)	80	85	88	100	100

* Denotes b. p.

Method of Estimation.—The olefin (*ca.* 2—3 × 10^{-3} mole) was weighed into the reaction vessel, which was placed in the bath until temperature equilibrium was attained. A pre-heated solution of the appropriate perbenzoic acid (*ca.* 6—8 × 10^{-2}M) was added to the mark, and the mixture was shaken vigorously. Aliquot portions (5 ml.) were withdrawn at determined times and added to 0·5N-potassium iodide (5 ml.) and 2N-sulphuric acid (10 ml.). The liberated iodine was titrated with 0·08N-sodium thiosulphate (starch). The perbenzoic acids were also estimated in this way. When diethyl ether was used as solvent, it was necessary to add carbon tetrachloride to the titration mixture in order to obtain satisfactory end-points (cf. Lynch and Pausacker, *loc. cit.*).

Results.—Reactions were followed in the range 0—60% completion, and were found to obey second-order kinetics. The rate constants, calculated by standard methods, obeyed the Arrhenius equation.

The reaction of *trans*-stilbene with perbenzoic acid in benzene at 30° is given as a typical example in Table 1.

TABLE 1.

Initial olefin concn. = 0·04932M (7·00 ml. of 0·07043N-$Na_2S_2O_3$)
Initial perbenzoic acid concn. = 0·06416M (9·11 ml. of 0·07043N-$Na_2S_2O_3$)
First perbenzoic acid estimation = 8·94 ml.
Equiv. olefin concn. = 6·83 ml.

Time (min.)	12·0	36·3	70·8	106·0	155·0	216·5	303·0
Titre (ml.)	8·86	8·69	8·48	8·27	7·99	7·64	7·28
10^4k_2 (mole^{-1} l. sec.$^{-1}$)	2·59	2·75	2·68	2·69	2·71	2·74	2·71

Mean: k_2 = 2·70 × 10^{-4} mole^{-1} l. sec.$^{-1}$.

Results obtained at different temperatures are:

Temp.	20°	25°	30°	35°
10^4k_2 (mole^{-1} l. sec.$^{-1}$)	2·69, 2·70	4·25, 4·29	6·56, 6·72	10·2, 10·1

The bimolecular constants obey the Arrhenius equation, as shown by the following data (the calculated values are given by $k = 1{\cdot}78 \times 10^8 e^{-15,800/RT}$):

Temp.		20°	25°	30°	35°
10^4k_2:	obs.	2·69$_5$	4·27	6·64	10·1$_5$
	calc.	2·70	4·28	6·68	10·3

(a) *Reactions in benzene.* The results obtained with the various olefins and perbenzoic acids in benzene are summarised in Table 2, duplicates being shown. $\Delta F^{\ddagger}$ and $\Delta H^{\ddagger}$ are in kcal. and $\Delta S^{\ddagger}$ in cal. deg.$^{-1}$. $\Delta F^{\ddagger}$ and $\Delta S^{\ddagger}$ for the various reactions are calculated from the rates at 30°.

TABLE 2. *Oxidation of olefins with substituted perbenzoic acids.*

(i) trans-*Stilbenes and perbenzoic acids.*

Substituted stilbene	Substituted perbenzoic acid	10^4k (mole^{-1} l. sec.$^{-1}$) 20°	25°	30°	35°	40°	$\Delta H^{\ddagger}$	$\Delta F^{\ddagger}$	$-\Delta S^{\ddagger}$
4 : 4′-$(OMe)_2$	Nil	—	83·6	128	180	270	14·0	20·4	21·1
			83·0	128	182	277			
4-OMe	Nil	13·0	20·2	31·2	48·0	—	14·5	21·2	22·3
		13·2	20·2	31·5	48·0				
4-Me	Nil	6·17	9·72	15·0	22·5	—	15·0	21·7	22·2
		6·17	9·64	14·7	23·2				
3-Me	Nil	3·07	4·80	7·41	11·3	—	15·2	22·1	22·7
		3·03	4·85	7·50	11·8				
Nil	Nil	2·69	4·25	6·72	10·2	—	15·2$_5$	22·2	22·8
		2·70	4·29	6·56	10·1				
4-Cl	Nil	1·70	2·68	4·22	6·53	—	15·6	22·4$_5$	22·6
		1·72	2·70	4·33	6·56				
3-Cl	Nil	1·04	1·74	2·73	4·25	—	15·9$_5$	22·7	22·2
		1·07	1·79	2·79	4·31				
3-NO_2	Nil	—	0·70	1·12	1·70	2·68	16·4	23·2$_5$	22·6
			0·75	1·16	1·70	2·63			
4-NO_2	Nil	—	0·62	0·98	1·51	2·30	16·6$_5$	23·3	22·0
			0·64	0·97	1·60	2·50			
Nil	4-NO_2	29·5	44·4	66·8	97·5	—	13·8	20·8	23·1
		29·0	44·0	66·2	98·0				
4-NO_2	4-NO_2	3·40	5·31	8·25	12·4	—	15·1	22·0	22·7
		3·40	5·41	8·28	12·5				
Nil	3-NO_2	26·4	39·2	58·9	89·0	—	13·9	20·8$_5$	23·0
		27·1	39·7	59·0	89·0				
Nil	3-Cl	9·90	15·0	23·1	34·2	—	14·5$_5$	21·4	22·9
		9·95	15·0	23·5	33·7				
Nil	4-Cl	6·51	10·2	15·1	24·6	—	14·9	21·6$_5$	22·4
		6·80	10·5	16·0	23·6				
Nil	4-Me	—	2·39	3·73	5·63	8·41	15·6	22·5	22·9
			2·37	3·78	5·66	8·58			
Nil	4-OMe	0·81	1·30	2·12	3·40	—	16·0$_5$	23·0	22·8
		0·82	1·35	2·20	3·50				

(ii) *Other olefins and perbenzoic acid.*

Olefin	10^4k (mole^{-1} l. sec.$^{-1}$) 20°	25°	30°	35°	40°	$\Delta H^{\ddagger}$	$\Delta F^{\ddagger}$	$-\Delta S^{\ddagger}$
Styrene	6·12	9·64	14·0	21·2	—	14·2	21·7	24·8
	6·20	9·65	14·4	21·4				
cis-Stilbene	5·70	8·96	13·0	19·6	—	14·1	21·7$_5$	25·2
	5·80	8·74	13·7	19·7				
Triphenylethylene ...	—	2·05	3·07	5·02	7·01	15·7	22·6	22·7
		2·06	3·08	5·00	7·40			
Tetraphenylethylene	—	—	0·27	0·45	0·79	17·2	24·1	22·6
			0·29	0·43	0·79			
*cyclo*Hexene	127	180	264	360	—	12·7	19·9$_5$	24·0
	127	182	263	365				

(b) *Reactions in diethyl ether.* Only the reactions of *trans*-stilbene and *cyclo*hexene with perbenzoic acid were investigated in ether. The reactions were of second order and the rates of reaction obeyed the Arrhenius equation. Summarised results (units as before) are :

Olefin	10^4k (mole^{-1} l. sec.$^{-1}$) 15°	20°	25°	28°	30° (calc.)	$\Delta H^{\ddagger}$	$\Delta F^{\ddagger}$	$-\Delta S^{\ddagger}$
trans-Stilbene	0·17	0·29	0·50	0·67	0·84	17·9	23·4	18·2
	0·16	0·30	0·51	0·67				
*cyclo*Hexene	2·25	3·72	5·82	7·50	8·96	15·3	22·0	22·0
	2·20	3·75	5·85	7·50				

(c) *Acid-catalysis and salt effects.* The effect of added benzoic acid on the oxidation rate of *trans*-stilbene with perbenzoic acid in benzene was investigated at 30°. For a mixture

containing *trans*-stilbene ($5{\cdot}8 \times 10^{-2}$M) and perbenzoic acid ($6{\cdot}4 \times 10^{-2}$M), the following rates were observed in the presence of varying concentrations of benzoic acid :

Acid concn. (10^2M)	1·4	2·9	6·6	8·1
10^4k (mole^{-1} l. sec.$^{-1}$)	6·65	6·58	6·57	6·68

The effect of added salt on the oxidation rates of *trans*-stilbene and *cyclo*hexene by perbenzoic acid in diethyl ether at 25° was investigated by addition of magnesium perchlorate. Results were :

Olefin	Olefin concn. (M)	Peracid concn. (M)	$Mg(ClO_4)_2$ concn. (M)	10^4k (mole^{-1} l. sec.$^{-1}$)
trans-Stilbene	0·11	0·17	0·01	0·51, 0·51
*cyclo*Hexene	0·05	0·08	0·013	5·71, 6·07

Discussion

The entropy of activation is virtually constant for the reactions of *trans*-stilbenes with perbenzoic acids in benzene solution, so either the free energies of activation or the heats of activation may be used to interpret the effects of substituents on the electron density at the reacting centres, as differences in these quantities are then both equal to the potential-energy change for the reaction (Hammett, *op. cit.*, pp. 118 *et seq.*). Examination of the effects of the various substituents in these reactions shows that, although there are not very large changes in the free energies and heats of activation, electron-donating substituents in *trans*-stilbene decrease these quantities, whereas electron-accepting substituents increase them. With the substituted perbenzoic acids, however, electron-accepting substituents decrease, and electron-donating substituents increase, the free energies and heats of activation. The effect of substituents is more apparent when the rates (10^4k at 30°) are listed : (*a*) substituted *trans*-stilbenes with perbenzoic acid, 4 : 4′-$(OMe)_2$ (128) > 4-OMe (31·3) > 4-Me (14·8) > 3-Me (7·45) > Nil (6·64) > 4-Cl (4·22) > 3-Cl (2·76) > 3-NO_2 (1·14) > 4-NO_2 (0·98); (*b*) substituted perbenzoic acids with *trans*-stilbene, 4-NO_2 (66·5) > 3-NO_2 (59·0) > 3-Cl (23·3) > 4-Cl (15·5) > Nil (6·64) > 4-Me (3·75) > 4-OMe (2·16). The qualitative effects of substituents are therefore in accord with the characters of olefins and per-acids as nucleophilic and electrophilic reagents respectively (cf. Swern, *loc. cit.*).

Further, there are satisfactory linear relations between the logarithms of the rate constants (at 30°) and Hammett's "sigma" constant for the substituent (Hammett, *op. cit.*, pp. 184 *et seq.*), for the series of substituted *trans*-stilbenes and perbenzoic acids, and these are shown in Figs. 1 and 2. The methoxy-substituted compounds show the greatest divergences, which is not unusual (cf. Jaffé, *Chem. Rev.*, 1953, **53**, 191).

Comparison of the rates of epoxidation of *trans*-stilbene and of *cyclo*hexene by perbenzoic acid in diethyl ether and in benzene shows that the rates are much greater in benzene, with lower free energies and heats of activation. This would not be expected if the reaction is ionic, since the more polar diethyl ether would be expected to increase the rates and decrease the activation energies. The effect of solvent in this reaction is similar to that observed in the per-acid oxidation of phenylhydrazones (Lynch and Pausacker, *loc. cit.*) and alkyl sulphides (Overberger and Cummins, *loc. cit.*), but is in contrast to that in the per-acid oxidation of ketones where the rates increase with increasing polarity of the solvent (Friess and Pinson, *J. Amer. Chem. Soc.*, 1952, **74**, 1302).

Addition of magnesium perchlorate did not affect the oxidation rates of *trans*-stilbene or of *cyclo*hexene by perbenzoic acid in diethyl ether at 25°. This is consistent with the proposed mechanism of epoxidation, since the transition state is non-ionic, but eliminates any process involving ionisation of the per-acid as a rate-determining step.

Similarly, it was found that addition of benzoic acid to the oxidation mixture of *trans*-stilbene and perbenzoic acid in benzene at 30° did not affect the rate of oxidation within experimental error. This is in contrast to Swern's assertion (*op. cit.*, p. 385) that "per-acid oxidations so far investigated are subject to general acid-catalysis," although Boeseken and Stuurman (*loc. cit.*) and Medvedev and Blokh (*loc. cit.*) found that oxidations of olefins by peracetic acid in acetic acid, and by perbenzoic acid in xylene, were not acid-catalysed.

The observed second-order kinetics in all the reactions studied shows, furthermore, that the benzoic acid formed as a reaction product does not catalyse the reaction. However, it has been shown (Friess, *J. Amer. Chem. Soc.*, 1949, **71**, 2571; Friess and Soloway, *ibid.*, 1951, **73**, 3968) that the reactions of per-acids with ketones are acid-catalysed, as with many other addition reactions of carbonyl compounds. Swern has drawn his examples of acid-catalysed per-acid oxidations from this class of reaction, but they are not relevant to the mechanism of epoxidation.

The reactivity towards perbenzoic acid of the series of phenyl-substituted ethylenes follows the double-bond orders of the olefinic links (*i.e.*, styrene > *trans*-stilbene > triphenylethylene > tetraphenylethylene) as calculated by Coulson and Jacobs (*J.*, 1949, 2805). In epoxidation, therefore, it may be postulated that perbenzoic acid acts as a "double-bond reagent" (Badger, *Quart. Rev.*, 1951, **5**, 147), *i.e.*, that reaction involves

FIG. 1. *Relation between the rate constant at 30° and the Hammett "sigma" constant for reaction of perbenzoic acid with substituted* trans*-stilbenes.*

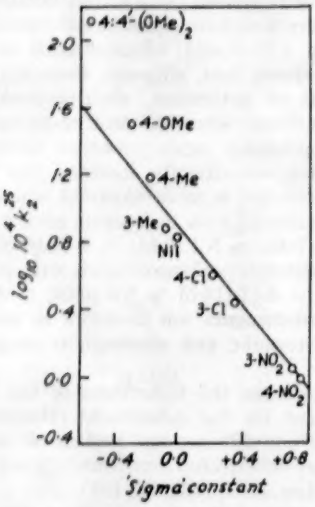
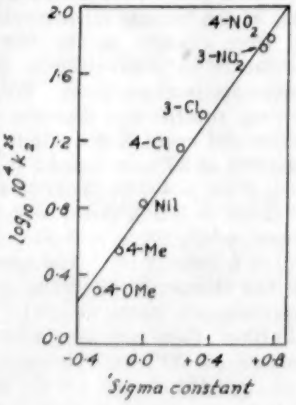
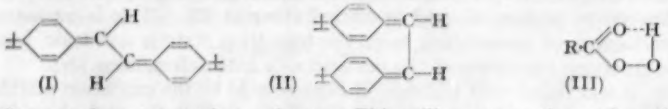


FIG. 2. *Relation between the rate constant at 30° and the Hammett "sigma" constant for reaction of* trans*-stilbene with substituted perbenzoic acids.*



attack on the olefinic bond and not on one of the constituting carbon atoms. Support for this is furnished by the virtual identity of the rates of epoxidation of 2-methylpropene and but-2-ene by peracetic acid in acetic acid solution (Boeseken and Stuurman, *loc. cit.*).

The structure of *trans*-stilbene has been determined by *X*-ray methods (Robertson, Prasad, and Woodward, *Proc. Roy. Soc.*, 1936, *A*, **154**, 187; Robertson and Woodward, *ibid.*, 1937, *A*, **162**, 568; *J.*, 1936, 1817), which show that the molecule is planar. Owing to contributions of structure (I) to the resonance hybrid, the olefinic bond will have some single-bond character, so that the electron density at this bond will be below that expected in the absence of conjugation. With *cis*-stilbene, however, scale models and scale diagrams



show that the two rings cannot be coplanar. This will suppress the conjugation, so that structures of type (II) can make no appreciable contribution to the normal state of the molecule. The electron density around the olefinic link will therefore be much greater than that in the *trans*-compound (cf. *cis*- and *trans*-azobenzene; Badger, Buttery, and Lewis, *J.*, 1953, 2145). It would be expected, therefore, that *cis*-stilbene would be

epoxidised more rapidly than *trans*-stilbene, and this is confirmed by the results shown in Table 2. The free energy and the heat of activation are lower for *cis*-stilbene, which is epoxidised at almost the same rate as styrene.

The proposed mechanism is further supported by recent investigations of the infra-red absorption spectra of the organic per-acids. Measurements by Davison (*J.*, 1951, 2456), Giguere and Olmos (*Canad. J. Chem.*, 1952, **30**, 821), and Minkoff (*Proc. Roy. Soc.*, 1954, *A*, **224**, 176) show that per-acids exist in solution very largely in the monomeric, intramolecularly hydrogen-bonded form (III). The increased volatility of the per-acids compared with the corresponding carboxylic acids is probably due to this intramolecular chelation, which renders impossible the characteristic dimerisation noted with the carboxylic acids.

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Immunopolysaccharides. Part III. The Dimethyl Ethers of* L-*Rhamnopyranose.*

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The nature of a di-*O*-methyl-L-rhamnopyranose, obtained from a methyl ether of the *Pneumococcus* Type II specific polysaccharide by hydrolysis, has been investigated. It was distinguished from the known 2 : 3- and 3 : 4-di-*O*-methyl-L-rhamnopyranose by chemical and other studies and was identified as the one remaining structural isomer, 2 : 4-di-*O*-methyl-L-rhamnose. Its synthesis from methyl 4-*O*-methyl-α-L-rhamnopyranoside has been achieved by a method involving the formation and controlled methanolysis of trifluoroacetyl derivatives.

L-RHAMNOSE was first recognised as a constituent sugar of the *Pneumococcus* Type II specific polysaccharide by Stacey (*Quart. Rev.*, 1947, **1**, 217) in 1947, and since that time its presence has been confirmed by Beiser, Kabat, and Schor (*J. Immunol.*, 1952, **69**, 297) and by Butler and Stacey (following paper) who have carried out a preliminary structural investigation of the polysaccharide. From the products of hydrolysis of the methylated polysaccharide there was isolated a di-*O*-methyl-L-rhamnose (A), further methylation of which followed by acidic hydrolysis gave the known 2 : 3 : 4-tri-*O*-methyl-L-rhamnose which established that the diether was unsubstituted at $C_{(3)}$. In order that the diether might be assigned a definite structure comparative studies were made with the known 2 : 3- and 3 : 4-di-*O*-methyl-L-rhamnose and are described below.

3 : 4-Di-*O*-methyl-L-rhamnose was obtained by the method of Haworth, Hirst, and Miller (*J.*, 1929, 2469) while for the synthesis of the 2 : 3-derivative reference was made to the work of Brown, Hough, and Jones (*J.*, 1950, 1125). Methyl 4-*O*-benzoyl-2 : 3-di-*O*-methyl-α-L-rhamnopyranoside, prepared by complete methylation of methyl 4-*O*-benzoyl-α-L-rhamnopyranoside with silver oxide and methyl iodide, was hydrolysed with aqueous-alcoholic alkali. The resulting glycoside gave 2 : 3-di-*O*-methyl-L-rhamnose in good yield on acidic hydrolysis, and it was shown to contain a minute amount of the 3 : 4-diether owing presumably to migration of the benzoyl group during methylation. This will be the subject of a subsequent communication. The 2 : 3-diether was purified by conversion into the crystalline aniline derivative (Percival and Percival, *J.*, 1950, 690) and regeneration on treatment of the latter with benzaldehyde.

* Part II, *J.*, 1954, 2395.

The dimethylrhamnose (A) and 3 : 4-di-*O*-methyl-L-rhamnose had the same melting point and the melting points of mixtures of the two were variable. However, appreciable differences between the specific rotations of the three diethers were found. On the paper chromatogram 2 : 3-di-*O*-methyl-L-rhamnose was readily distinguished by its slow rate of movement and red colour reaction with aniline trichloroacetate reagent (Brown *et al.*, *loc. cit.*). Mixtures of the 2 : 3-diether with each of the other two were separated in a reasonably satisfactory way for, although slight overlapping of the spots sometimes occurred, the component sugars could be recognised by their distinctive colours (A, brown; 3 : 4-, green-brown). On the other hand but little separation of (A) and the 3 : 4-diether could be achieved. The use of paper ionophoresis in borate buffer (Foster, *Chem. and Ind.*, 1952, 828) led to rapid and complete separation of 3 : 4-di-*O*-methyl-L-rhamnose from the other two ethers.

Confirmation that ether (A) presented no contiguous hydroxyl groups was given by its failure to reduce sodium metaperiodate. Under similar conditions the 3 : 4-diether consumed 1 mol. of the oxidising agent, a result in agreement with the value given by Hirst, Hough, and Jones (*J.*, 1949, 3145) but at variance with that of Brown *et al.* (*loc. cit.*) (0·7 mol.). The latter group state that 2 : 3-di-*O*-methyl-L-rhamnose is oxidised to the extent of 0·1 mole/mole.

Properties of the di-O-methyl-L-rhamnopyranoses and their derivatives.

		Free sugar						*N*-Phenylglycosylamine		2 : 4-Dinitrophenylhydrazone	
L-Rhamnose ether		M. p.	$[\alpha]_D^{20}$ in H_2O	R_G	Colour *	M_G	P †	M. p	$[\alpha]_D^{20}$ in EtOH	M. p.	$[\alpha]_D^{20}$ in dioxan
2 : 3-Me_2	Syrup	—	44·3°	0·83	Red	0·02	0·0	136—137°	147·8 → 42·8	168°	45·4°
2 : 4-Me_2	Hygroscopic solid	91—93°	10·6	0·87	Brown	0·02	0·0	141—142·5°	136 → 4	164—165	39·0
3 : 4-Me_2	Needles	91—92	18·0 (equ^{m})	0·88	Green-brown	0·4	1·0	—	—	170	75·6

All rotations are positive in degrees.

* On development with aniline trichloroacetate. † Periodate consumed (mole/mole).

The three diethers formed crystalline 2 : 4-dinitrophenylhydrazones having very similar melting points: these were differentiated by their mixed melting points and their specific rotations. The ether (A) furnished a *N*-phenylglycosylamine which was distinguished from the corresponding derivative of 2 : 3-di-*O*-methyl-L-rhamnose by its optical rotational behaviour in methanol and by the mixed melting point. No crystalline *N*-phenylglycosylamine could be prepared from the 3 : 4-diether nor a crystalline phenylosazone from ether (A).

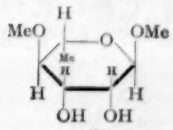
From these results, which are summarised in the Table, it was evident that the ether (A) was the other possible isomeric di-*O*-methylrhamnopyranose, *viz.*, the 2 : 4-derivative. This conclusion was supported by a synthesis of the sugar achieved as described below and already briefly described (Butler, Lloyd, and Stacey, *Chem. and Ind.*, 1954, 107).

Methyl 2 : 3-*O*-*iso*propylidene-α-L-rhamnopyranoside was prepared by Levene and Muskat's method (*J. Biol. Chem.*, 1934, **105**, 431) employing sulphuric acid and anhydrous copper sulphate as condensing agents. Use of zinc chloride gave lower yields but in one experiment the product was obtained crystalline, with m. p. 36°, $[\alpha]_D^{20}$ −15·9° (*c*, 1·6 in acetone), which has not been previously reported. Methylation with methyl iodide and silver oxide, followed by removal of the ketal grouping with methanolic hydrogen chloride, yielded hygroscopic prisms of methyl 4-*O*-methyl-α-L-rhamnopyranoside (I), from which with trifluoroacetic anhydride in the presence of sodium trifluoroacetate (Bourne, Tatlow, and Tatlow, *J.*, 1950, 1367) methyl 4-*O*-methyl-2 : 3-bis-*O*-trifluoroacetyl-α-L-rhamnopyranoside (II) was obtained in good yield.

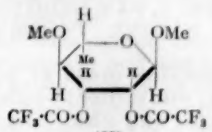
In its reaction with methanol the trifluoroacetate (II) resembled other trifluoroacetates previously reported (Bourne, Tatlow, and Tatlow, *loc. cit.*), dissolution in the alcohol

leading to complete deacetylation with quantitative regeneration of the ether (I). The de-esterification was remarkably rapid and, as indicated polarimetrically, was complete after about 25 min. at room temperature. The method of partial removal of trifluoroacetyl employed by Bourne, Stacey, Tatlow, and Tatlow (*J.*, 1951, 826) was inapplicable to synthesis of the 3 : 4-dimethyl ether owing to the high solubility in alcohol of the methyl rhamnosides. Attempts to precipitate a monotrifluoroacetate from various alcoholysis reagents with light petroleum or carbon tetrachloride were unsuccessful. Trial experiments indicated that very little methanolysis occurred in the presence of a large excess (6 volumes) of carbon tetrachloride from which the alcohol could be rapidly removed by distillation under reduced pressure.

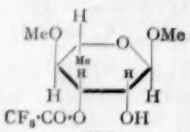
When de-esterification was conducted in methanol–carbon tetrachloride (65 : 35 v/v), the final product, recovered by evaporation, was again methyl 4-*O*-methylrhamnoside (I). When the methanolysis was effectively terminated at the point of maximum optical rotation, by pouring into a large volume of carbon tetrachloride, there was obtained, on evaporation of the solvent, a syrup which had the methoxyl content of a monotrifluoroacetate (III). During the early stages of methanolysis, starting material could be isolated from the reaction mixture. As deacylation proceeded this became more difficult and after a time only syrups could be obtained. This point was always reached well before the mixture had attained maximum optical rotation and, since the diester (II) was normally readily crystallisable, even in the presence of an equal weight of the diol (I), much more rapid de-esterification of the diester than of the monotrifluoroacetate(s) was again indicated. From the form of the methanolysis curve it seemed likely that the monoester obtained was essentially a single molecular species rather than a mixture of the 2- and the 3-monotrifluoroacetate. The methanolysis curve was reproducible and curves of similar form were recorded on replacement of the carbon tetrachloride with other diluents such as chloroform or ether, the rate of methanolysis being related to the concentration of methanol employed. It was clear that when pure methanol was used reaction occurred so rapidly that the initial increase in optical rotation could not be accurately recorded.



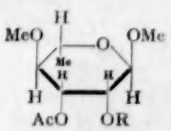
(I)



(II)



(III)



(IV); R = H
(V); R = Me

The monotrifluoroacetate (III) was acetylated with pyridine and acetic anhydride, and methanolysis of the product afforded syrupy methyl 3-*O*-acetyl-4-*O*-methyl-α-L-rhamnoside (IV). This was converted into methyl 3-*O*-acetyl-2 : 4-di-*O*-methyl-α-L-rhamnoside (V) by silver oxide and methyl iodide and then, after Zemplen deacetylation, into the reducing sugar by acidic hydrolysis. The main product, as determined chromatographically, was a dimethyl-L-rhamnose and this was separated from traces of 4-*O*-methyl- and tri-*O*-methyl-L-rhamnose by chromatography on paper strips. It was predominantly 2 : 4-di-*O*-methyl-L-rhamnose but ionophoresis (Foster, *loc. cit.*) revealed that a small amount of 3 : 4-di-*O*-methyl-L-rhamnose was also present.

On treatment with hot ethanolic aniline the product formed crystalline 2 : 4-di-*O*-methyl-*N*-phenyl-L-rhamnosylamine identical with that derived from the methylated *Pneumococcus* Type II polysaccharide. On acid hydrolysis the rhamnosylamine yielded a product showing M_G 0·02 and no trace of 3 : 4-di-*O*-methyl-L-rhamnose (M_G 0·4). The method of synthesis precluded the formation of any 2 : 3-di-*O*-methyl-L-rhamnose; the structure assigned to the dimethyl rhamnose from the Type II *Pneumococcus* was thus fully confirmed.

The above synthesis was not quite so unequivocal as that of Bourne, Stacey, Tatlow, and Tatlow (*loc. cit.*) in the glucose series. An analogous reaction sequence was involved and we consider the mechanism of the displacement of the residual trifluoroacetyl groups

from $C_{(3)}$ to $C_{(2)}$ is the same. Of the possible mechanisms by which removal of trifluoroacetyl (methanolysis) could proceed, the rate-controlling step would be a nucleophilic attack by MeO^- or $MeO^\delta{}^-$, $H^{\delta+}$. This would be aided by an electrophilic substituent at the α-position in the alcohol. Thus methanolysis would be expected to proceed more rapidly at $C_{(2)}$, to which is attached the strongly electronegative, potentially reducing group, than at $C_{(3)}$. This interpretation would also explain the relatively high stability of monotrifluoroacetates compared with that of polyesters with adjacent trifluoroacetyl groups (Bourne, Tatlow, and Tatlow, *loc. cit.*).

The monotrifluoroacetate obtained by selective methanolysis of the diester (II) is regarded as having the structure, methyl 4-*O*-methyl-3-*O*-trifluoroacetyl-α-L-rhamnoside (III). Thus in order to obtain the monoacetate (V), and finally the 2 : 4-diether (A), migration of an acyl group must occur at some stage. This may have taken place during methylation (IV ⟶ V) but it is considered more likely that transposition of the trifluoroacetyl group occurred during acetylation of (III), as has been observed in the glucose series.

It is now recognised that the spatial orientation of substituents in pyranoside sugars may be an important factor in determining rates of interaction (cf. Foster, Martlew, and Stacey, *Chem. and Ind.*, 1953, 825). Even in unimolecular reactions steric effects may be very considerable (Newth and Phillips, *J.*, 1953, 2904) and it is likely that the rates of methanolysis of carbohydrate trifluoroacetates are in some measure governed by stereochemical factors. However, until a wider, quantitative study has been made, not only of reaction rates but also of reaction mechanism, analysis in such terms of the cases under discussion would be premature.

Experimental

Unless otherwise stated, all operations involving trifluoroacetates were conducted with dry reagents under anhydrous conditions.

2 : 3-*Di*-O-*methyl*-N-*phenyl*-L-*rhamnosylamine*.—Slightly impure 2 : 3-di-*O*-methyl-L-rhamnose prepared by essentially the method of Brown, Hough, and Jones (*loc. cit.*) was converted according to Percival and Percival's directions (*loc. cit.*) into the *N*-phenylrhamnosylamine, m. p. 136—137°, $[\alpha]_D^{20}$ +147·8° ⟶ +42·8° in 70 hr. (*c*, 0·4 in EtOH) (Found: C, 63·2; H, 7·8; N, 5·4. Calc. for $C_{14}H_{21}O_4N$: C, 62·9; H, 7·9; N, 5·2%). Percival and Percival gave m. p. 138—139°.

2 : 3-*Di*-O-*methyl*-L-*rhamnose*.—The above derivative (0·036 g.) was treated with water (6 ml.) and freshly distilled benzaldehyde (0·066 g.) with stirring by carbon dioxide; the mixture was heated at 90° for 1½ hr., cooled, and extracted with ether. Evaporation of the aqueous solution gave syrupy 2 : 3-di-*O*-methyl-L-rhamnose, which was chromatographically and ionophoretically homogeneous and had $[\alpha]_D^{21}$ +44·3° (*c*, 0·8 in H_2O). Schmidt, Plankenhorn, and Kubler (*Ber.*, 1942, **75**, 579) gave $[\alpha]_D$ +47·7°, Percival and Percival $[\alpha]_D$ +40°, and Brown, Hough, and Jones $[\alpha]_D$ +42·5°.

Properties of 2 : 3-, 2 : 4-, *and* 3 : 4-*Di*-O-*methyl*-L-*rhamnose*.—The three compounds were examined together on paper chromatograms, the mobile phase being the organic layer of *n*-butanol–ethanol–water (4 : 1 : 5), and the developer aniline trichloroacetate. For R_G values and colours see the Table, which includes M_G values obtained by ionophoresis in borate buffer at pH 10 (Foster, *loc. cit.*).

Weighed samples of 2 : 4- and 3 : 4-di-*O*-methyl-L-rhamnose were treated with standard (0·25M or 0·15M) sodium metaperiodate at room temperature. The extent of oxidation was determined by treatment with excess of sodium hydrogen carbonate followed by potassium iodide solution and titration of the liberated iodine with sodium arsenite (Muller and Friedberger, *Ber.*, 1902, **35**, 2652). 3 : 4-Di-*O*-methyl-L-rhamnose utilised 1·00, 1·03 mols. after 3 hr. and 1·00 mol. after 3·5 hr., and 2 : 4-di-*O*-methyl-L-rhamnose 0·01 mol. after 3 or 5 hr. Control determinations were in close agreement.

2 : 4-*Di*-O-*methyl*-L-*rhamnose* 2 : 4-*Dinitrophenylhydrazone*.—2 : 4-Di-*O*-methyl-L-rhamnose (0·120 g.) was heated with 2 : 4-dinitrophenylhydrazine (0·065 g.) in 50% (v/v) acetic acid (0·84 ml.) at 90° for 12 min. On cooling lemon-yellow needles were deposited. Water (2·1 ml.) was added, and after 3 hr. at room temperature the precipitate was filtered off and washed with water. Recrystallisation from ethanol afforded the 2 : 4-*dinitrophenylhydrazone* (0·070 g.), m. p. 164—165° (decomp.), $[\alpha]_D^{23}$ +39·0° (*c*, 1·0 in dioxan) (Found: C, 45·4; H, 5·6; N, 15·3. $C_{14}H_{20}O_8N_4$ requires C, 45·2; H, 5·4; N, 15·1%).

2 : 3-*Di*-O-*methyl*-L-*rhamnose 2 : 4-*Dinitrophenylhydrazone*.—2 : 3-Di-*O*-methyl-L-rhamnose formed a hydrazone less readily than the 2 : 4-isomer, requiring 45 min. at 90—95° under the above conditions. The product separated as an orange oil which slowly crystallised on trituration and addition of water and recrystallised as lemon-yellow needles, m. p. 168° (decomp.), $[\alpha]_D^{23}$ +45·4° (*c*, 0·6 in dioxan), from a small volume of ethanol (Found : C, 44·9; H, 5·6; N, 15·4%).

3 : 4-*Di*-O-*methyl*-L-*rhamnose 2 : 4-*Dinitrophenylhydrazone*.—A solution of 3 : 4-*O*-methyl-L-rhamnose (0·110 g.) in 50% acetic acid (0·94 ml.) was heated with 2 : 4-dinitrophenylhydrazine (0·075 g.) on the water-bath at 50° for 65 min. The mixture was cooled and the material in suspension (hydrazone and some unchanged hydrazine) was removed, washed with water, and recrystallised from ethanol, yielding **3 : 4-*di*-O-*methyl*-L-*rhamnose 2 : 4-*dinitrophenylhydrazone*** (0·044 g.), lemon-yellow needles, m. p. 170° (decomp.), $[\alpha]_D^{23}$ +75·6° (*c*, 1·0 in dioxan) (Found : C, 45·1; H, 5·6; N, 15·5%).

Admixture of any two of the above described 2 : 4-dinitrophenylhydrazones depressed the m. p. by about 20°.

2 : 4-*Di*-O-*methyl*-N-*phenyl*-L-*rhamnosylamine*.—Treatment of 2 : 4-di-*O*-methyl-L-rhamnose (0·170 g.) with aniline (0·120 g.) in boiling ethanol (2·0 ml.) for 4 hr. followed by removal of the solvent in a vacuum-desiccator gave a *L-rhamnosylamine* (0·076 g.), m. p. 141—142·5° after recrystallisation from light petroleum (b. p. 40—60°), $[\alpha]_D^{18}$ +136° ⟶ +4° in 24 hr. (*c*, 0·5 in EtOH) (Found : C, 62·9; H, 7·7; N, 5·3; OMe, 23·1. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9; N, 5·2; OMe, 23·2%).

Methyl **4-O-*Methyl*-α-L-*rhamnopyranoside*.**—Methyl 4-*O*-methyl-2 : 3-*O*-*iso*propylidene-α-L-rhamnopyranoside (Levene and Muskat, *loc. cit.*) (6·4 g.) was heated in dry methanol (235 ml.), containing 1% of hydrogen chloride, under reflux for 1 hr. The solution was neutralised with silver carbonate, filtered, boiled with charcoal, filtered again, and evaporated in a vacuum to a colourless syrup. This crystallised on trituration with ether and exhaustive recrystallisation from ether–light petroleum (b. p. 60—80°) and finally from ether furnished ***methyl* 4-O-*methyl*-α-L-*rhamnopyranoside*** (2·5 g.) as hygroscopic white needles, m. p. 60—61°, $[\alpha]_D^{18}$ −87·3° (*c*, 1·1 in MeOH) (Found : C, 50·3; H, 8·6; OMe, 32·0. $C_8H_{16}O_5$ requires C, 50·0; H, 8·3; OMe, 32·3%).

Methyl 4-O-*Methyl*-2 : 3-*bis*-O-*trifluoroacetyl*-α-L-*rhamnopyranoside*.—Methyl 4-*O*-methyl-α-L-rhamnopyranoside (1·01 g.), when added to the gelatinous mixture of trifluoroacetic anhydride (3·3 ml.) and sodium trifluoroacetate (0·35 g.), underwent immediate vigorous reaction and required use of a reflux condenser. After 1 hr. at room temperature, the mixture was heated under reflux for 50 min., then distilled under slight vacuum with several portions of carbon tetrachloride until trifluoroacetic acid was no longer detectable. The residue was extracted with carbon tetrachloride and evaporation of the filtered extracts gave pale crystals. Prisms of ***methyl* 4-O-*methyl*-2 : 3-*bis*-O-*trifluoroacetyl*-α-L-*rhamnopyranoside*** (1·564 g.), obtained from light petroleum (b. p. 100—120°), had m. p. 98·5—99°, $[\alpha]_D^{16}$ −51·6° (*c*, 2·0 in $CHCl_3$) (Found : C, 37·7; H, 3·8; F, 28·3; OMe, 16·2. $C_{17}H_{14}O_7F_6$ requires C, 37·5; H, 3·7; F, 29·7; OMe, 16·2%). It could also be purified by sublimation, was soluble in the common organic solvents (but decomposed in alcohols) and insoluble in water, was stable for long periods when carefully purified and stored *in vacuo* over P_2O_5, but slowly decomposed in air.

Methanolysis.—(*a*) *In methanol.* Reaction of the bistrifluoroacetate (0·050 g.) in methanol (4·00 ml.) was followed by means of the change in optical rotation. The solvent was then removed under reduced pressure. The residual colourless methyl 4-*O*-methyl-α-L-rhamnopyranoside crystallised under ether and had m. p. and mixed m. p. 58—59° (Found : OMe, 32·8%).

(*b*) *In methanol–carbon tetrachloride* (65 : 35, *v*/*v*). Methanolysis of the diester in methanol–carbon tetrachloride (65 : 35, v/v) was followed polarimetrically. Periodically aliquot parts were mixed with 6 vols. of carbon tetrachloride and the solvents removed in a vacuum. Before maximum optical rotation had been reached, syrups or partly crystalline mixtures were obtained from which some starting material could be isolated during the early stages of methanolysis. Working up at the point of maximum rotation gave syrupy ***methyl* 4-O-*methyl*-3-O-*trifluoroacetyl*-α-L-*rhamnopyranoside***, $[\alpha]_D^{21}$ −75·8° (*c*, 1·2 in $CHCl_3$) (Found : OMe, 21·7. $C_{10}H_{15}O_6F_3$ requires OMe, 21·5%). After maximum rotation had been reached the product was methyl 4-*O*-methyl-α-L-rhamnopyranoside, the yield being quantitative when the rotation had become constant.

Methyl 3-O-*Acetyl*-4-O-*methyl*-α-L-*rhamnopyranoside*.—Acetic anhydride (0·36 ml.) was added to a solution of methyl 4-*O*-methyl-3-*O*-trifluoromethyl-α-L-rhamnopyranoside (0·70 g.) in pyridine (1·8 ml.). After 2 days at room temperature the volatile components were removed by distillation and co-distillation with carbon tetrachloride under diminished pressure and the

residual syrup was dissolved in methanol–carbon tetrachloride (3 : 1, v/v) (10 ml.) and kept at room temperature until the rotation became constant, the changes being : $[\alpha]_D^{20}$ −39·4° (initial); −38·7° (0·5 hr.); −37·2° (1 hr.); −33·9° (4 hr.); −31·7° (20 hr.); −31·7° (24 hr.). After evaporation the syrup (0·54 g.) obtained contained only a trace of fluorine [sodium fusion and treatment with cerous nitrate (Simons and Ramler, *J. Amer. Chem. Soc.*, 1943, **65**, 389)]. The *ester* had $[\alpha]_D^{21}$ −55·4° (*c*, 1·0 in $CHCl_3$) (Found : C, 49·7; H, 7·3; Ac, 19·0; OMe, 22·6. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7; Ac, 18·4; OMe, 26·5%).

Methyl 3-O-*Acetyl*-2 : 4-*di*-O-*methyl*-α-L-*rhamnopyranoside*.—The product from the previous experiment was methylated by two successive treatments with methyl iodide and silver oxide at 45° for 16 hr. The *product* had $[\alpha]_D^{22}$ −51·1° (*c*, 0·8 in $CHCl_3$) (Found : OMe, 37·1. $C_{11}H_{20}O_6$ requires OMe, 37·5%).

Methyl 2 : 4-*Di*-O-*methyl*-α-L-*rhamnopyranoside*.—The preceding syrupy methylation product (0·25 g.) was dissolved in dry methanol, and a small piece of sodium added. After 18 hr. the specific rotation had become constant and the solution was treated with solid carbon dioxide and evaporated to dryness, yielding a viscous amber *rhamnoside* (0·205 g.), $[\alpha]_D^{22}$ −68° (*c*, 4·1 in MeOH) (Found : OMe, 46·0. $C_9H_{18}O_5$ requires OMe, 45·1%).

2 : 4-*Di*-O-*methyl*-L-*rhamnose*.—A solution of the methyl di-*O*-methyl-L-rhamnopyranoside (0·190 g.) from the above experiment in 0·5N-hydrochloric acid (14·5 ml.) was heated on a boiling-water bath for 140 min.; the optical rotation had then become constant. The solution was neutralised with silver carbonate, filtered, and evaporated at 40—45° *in vacuo*, yielding an amber syrup (0·163 g.). On the paper chromatogram three spots were detected, the main component (R_G 0·86) corresponding to di-*O*-methyl-L-rhamnose. The other two spots, of much lower intensity, were due to mono- and tri-*O*-methyl-L-rhamnose (R_G 0·68, 0·99).

The di-*O*-methyl-L-rhamnose fraction was separated chromatographically on a larger scale employing 5 sheets (30 × 57 cm.) of Whatman No. 1 filter paper. A solution of the product in methanol was applied as a line of spots along the base line of each chromatogram. After irrigation for 17 hr. with *n*-butanol–ethanol–water (4 : 1 : 5; v/v) marginal and central strips were removed and developed. Horizontal strips containing the dimethyl sugar were cut from the remainders of the papers and extracted (Soxhlet) with ether. Evaporation of the extract furnished a viscous syrup (0·078 g.) which on drying *in vacuo* (P_2O_5) crystallised as hygroscopic fibrous needles, m. p. 80° (unsharply), $[\alpha]_D$ +3° (*c*, 1·0 in EtOH). Ionophoresis revealed, in addition to 2 : 4-di-*O*-methyl-L-rhamnose, a minute amount of 3 : 4-di-*O*-methyl-L-rhamnose.

Treatment of the product (0·065 g.) with ethanolic aniline as described above led to the formation of 2 : 4-di-*O*-methyl-*N*-phenyl-L-rhamnosylamine (0·010 g. after three recrystallisations), m. p. 141—142·5° alone or mixed with the specimen derived from the methylated Type II *Pneumococcus* polysaccharide. The samples showed similar optical rotational behaviour and had identical *X*-ray powder photographs (the latter investigation was kindly made by Dr. P. Cucka) (Found : C, 62·9; H, 7·9%).

Hydrolysis. The *N*-glycosylamine (0·5 mg.) was hydrolysed by N-hydrochloric acid at room temperature for 24 hr. A spot of the solution was transferred to the base line of an ionophoresis paper and there dried in a current of cold air. Ionophoresis showed M_G 0·02. No 3 : 4-di-*O*-methyl-L-rhamnose (M_G 0·4) was detected. A preliminary experiment using 2 : 3-di-*O*-methyl-*N*-phenyl-L-rhamnosylamine had indicated that under the conditions described above hydrolysis of the anilide to the parent sugar occurred.

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Immunopolysaccharides. Part IV. Structural Studies on the Type II* Pneumococcus *Specific Polysaccharide.*

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Acidic hydrolysis of a methylated derivative of the Type II *pneumococcus* specific polysaccharide revealed the presence of 2 : 4-di-*O*-methyl-L-rhamnopyranose (7 parts), 2 : 3-di-*O*-methyl-D-glucose (1 part), 2 : 3-di-*O*-methyl-D-glucuronic acid (2 parts), and 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid (1 part). The polysaccharide possesses a highly branched chain structure with D-glucose forming a large proportion of the branch points. The serological relation of the Type II polysaccharide to certain dextrans and other polyglucoses may be explained by the common presence in them of glucose units having the same spatial geometry at branch points.

Although the " soluble specific substance " of Type II *pneumococcus* was the first of the bacterial capsular materials to be recognised as a polysaccharide by Heidelberger and Avery (*J. Exp. Med.*, 1923, **38**, 73; 1924, **40**, 301) its fine structure remained undetermined in spite of the inherent chemical interest of these substances and their great importance for the understanding of bacterial specificity and immunity to infectious disease. However, the molecular structure of the more readily accessible specific polysaccharide of Type III *pneumococcus* has been shown by Reeves and Goebel (*J. Biol. Chem.*, 1941, **139**, 511) to be that of a polycellobiuronic acid with its units held by 1→3 linkages.

The present report deals with preliminary structural investigations on the Type II substance made possible by a generous sample of material prepared by E. R. Squibb and Sons, New Brunswick, N.J., U.S.A., and supplied through the courtesy of Professor M. Heidelberger and the Surgeon General of the United States Army.

The Type II polysaccharide has the property of cross-reacting specifically with Type III antiserum and this may be considered to be due to the fact that the Type II material possesses glucose (Heidelberger, *Chem. Rev.*, 1929, **3**, 403) and glucuronic acid units. Elegant methods for isolating the polysaccharide have been devised by Heidelberger, Kendall, and Scherp (*J. Exp. Med.*, 1936, **64**, 559). Eight-day broth cultures are usually made and the polysaccharide is precipitated by addition of 95% alcohol to the autolysed broth culture. It is freed from protein by Sevag's method (*Biochem. Z.*, 1934, **273**, 419) and from glycogen by addition of saliva.

In earlier studies of its physical properties, Record and Stacey (*J.*, 1948, 1561) have shown that it forms solutions of high viscosity in water, that its molecular weight is of the order of 240,000, and that it has a cylindrical molecule.

The material provided was essentially free from protein and glycogen. It did, however, contain small amounts of deoxypentosenucleic acid and glucosamine-containing material. It was readily freed from these by fractional precipitation with cetyltrimethylammonium bromide (Jones, *Biochem. Biophys. Acta*, 1953, **10**, 607).

Further fractionation was carried out by gradual addition of ethyl alcohol to aqueous solutions in the usual way. The resulting main fraction, $[\alpha]_D + 60°$, was electrophoretically homogeneous in the pH range 5·0—8·0, and was considered suitable for chemical examination.

The infrared spectrum indicated the possible presence of (1→4)-α- and (1→6)-α-glycosidic linkages, these α-linkages also being indicated by the downward trend of the specific rotation on acidic hydrolysis. The absence of furanose sugars was indicated by the fact that prolonged treatment with 0·01N-sulphuric acid at 95° failed to liberate any components detectable on a chromatogram. Chromatographic analysis of a more vigorously hydrolysed solution revealed four components. Two spots corresponded to D-glucurone and D-glucuronic acid while two others corresponded to D-glucose and to L-rhamnose.

* Part III, preceding paper.

Glucose had been recognised by Heidelberger (*loc. cit.*), and L-rhamnose had also been isolated and identified (Stacey, *Quart. Rev.*, **1947**, **1**, 217; Record and Stacey, *loc. cit.*; Beiser, Kabat, and Schor, *J. Immunol.*, **1952**, **69**, 297). The acidic nature of the polysaccharide was due to the glucuronic acid component which could be detected in hydrolysates by its strong colour reaction with naphtharesorcinol. The equivalent weight of the polysaccharide was estimated by conductometric titration to be *ca.* 1000, a figure largely in agreement with early published figures.

Methylation was smoothly accomplished with sodium hydroxide and methyl sulphate in the usual way, though the highest methoxyl content which could be introduced was only 42·0%.

Fractionation of the sodium salt of the methylated polysaccharide was achieved by precipitation from chloroform or aqueous solution by means of solvents and the major portion, an essentially homogenous material (OMe, 42·1%), was selected for methanolysis. This was carried out with 4% methanolic hydrogen chloride in sealed tubes at 100°. The resulting products were hydrolysed and then separated into four fractions by means of ion-exchange resins. The neutral methylated sugars were separated by partition chromatography. The first and major fraction was shown (as described by Butler, Lloyd, and Stacey, preceding paper) to consist of 2 : 4-di-*O*-methyl-L-rhamnopyranose and the second was identified as 2 : 3-di-*O*-methyl-D-glucopyranose.

The two acidic fractions each behaved as mixtures and appeared to contain aldobiuronic acid residues. They were combined and treated in a sealed tube with 5% methanolic hydrogen chloride at 100°.

Identification of the products by means of de-esterification, acid hydrolysis, and oxidation with bromine, etc., gave 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid (1 part), 2 : 3-di-*O*-methyl-D-glucuronic acid (2 parts), and 2 : 3-di-*O*-methyl-D-glucose (1 part). An assessment of the total amounts of the identified constituents revealed the approximate proportions as 2 : 4-di-*O*-methyl-L-rhamnopyranose (7 parts), 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid (1 part), 2 : 3-di-*O*-methyl-D-glucuronic acid (2 parts), and 2 : 3-di-*O*-methyl-D-glucose (1 part). Somewhat similar proportions were found by our former colleague Dr. P. W. Kent (*Chem. and Ind.*, **1952**, 1176) using a scanning method.

In the present state of the investigation any attempts at writing a formula for the repeating unit of polysaccharides are considered to be premature, and formulation of structure must await the securing of higher yields of the methyl ether and detailed examination of oligosaccharide fragments.

It is clear, however, that the structure is highly branched with some of the glycosidically linked glucuronic acid residues forming the ends of chains and having, as is usual, the carboxyl groups free. The L-rhamnose residues are all present in a chain structure while the D-glucose residues form the branch points in the molecule.

This occurrence of glucose residues as branch points with other residues linked through the 1→4 and 1→6 positions, may, as already suggested (Heidelberger and Aisenberg, *Proc. Nat. Acad. Sci.*, **1953**, **39**, **453**; Stacey, *Biochem. Soc. Symp.*, 1953, No. 10, p. 74) provide the key to an understanding of the long known cross reactivity of certain dextrans with Type II anti-*pneumococcus* serum (Sugg, Hehre, and Neill, *J. Bact.*, **1942**, **43**, 24; Neill and Abrahams, *Proc. Soc. Exp. Biol.*, **1951**, **78**, 537) and help to explain the reactivity of the dextrans in other antisera, the more so as glucose has now been recognised as a component of the specific polysaccharides of Types IX and XII *pneumococci* (Heidelberger, Barker, and Stacey, *Science*, **1954**, **120**, 781) in antisera to which dextrans and glycogens react strongly.

The present finding that the glucose in the Type II substance occurs as 1, 4, and 6 branch points also enabled Heidelberger and Aisenberg (*loc. cit.*) to predict from the quantitative theory of specific precipitation (Heidelberger and Kendall, *J. Exp. Med.*, **1935**, **61**, 563) that glycogen and amylopectin, which also contain multiple 1, 4, and 6 branch points of glucose, would precipitate Type II antiserum and to demonstrate (*J. Exp. Med.*, **1954**, **99**, **343**) that these polysaccharides of widespread occurrence show much the same distribution of cross reactivity in Type II and other anti-*pneumococcus* sera as do the dextrans. Heidelberger has also found that tamarind-seed polysaccharide (jellose),

in which two of the three glucose residues in the repeating unit of galactose, glucose, and xylose are linked in the **1**, **4**, and **6** positions, causes heavy precipitation with Type II anti-*pneumococcus* serum (" Perspectives in Microbiology," Rutgers Univ. Press, **1954**).

Experimental

Properties of the Polysaccharide.—The polysaccharide, prepared by essentially the method of Heidelberger, Kendall, and Scherp (*J. Exp. Med.*, **1936**, **64**, 559), was provided in the form of its sodium salt as a white powder, insoluble in organic solvents, but soluble in water forming highly viscous solutions, $[\alpha]_D^{18}$ +50° (*c*, 1·0).

Colorimetric tests on the hydrolysed polysaccharide gave the following results: biuret test for protein and iodine test for glycogen, negative; Dische's diphenylamine reagent (*Mikrochem.*, **1930**, **8**, 4) for nucleic acids and Ehrlich's test (Morgan and Elson, *Biochem. J.*, **1934**, **28**, 988) for amino-sugars, weakly positive; Tollens's reagent (naphtharesorcinol) for uronic acids, positive. It contained N 1·2, P 0·78, and ash 8·7%.

Treatment with cetyltrimethylammonium bromide and electrophoretic examination of aqueous solutions at pH 6·0 showed that *ca.* 6% of deoxyribonucleic acid was present in the polysaccharide (Stacey, *Ann. Acad. Sci. Fennicae*, 1955, *A*, **11**, 60, 262).

Three fractions were isolated when absolute ethanol was gradually added to a 3% aqueous solution which had been acidified to pH 3·8 with acetic acid. Their properties are compared in the Table.

Properties and composition of polysaccharide fractions.

Fractions	Wt. (g.)	$[\alpha]_D^{18}$	N (%)	P (%)	Ash (%)
A	0·17	+66°	1·5	0·80	4·3
B	0·46	+49	1·1	0·82	7·6
C	0·38	+47	1·1	—	5·7

Measurement of the specific viscosity of aqueous solutions of each fraction at concentrations ranging from 0·3% to 0·1% indicated that they were reasonably homogeneous in regard to molecular weight. The fractions were mixed with a larger sample of polysaccharide, dissolved in water, and treated with cetyltrimethylammonium bromide according to the method of Jones, Dutta, and Stacey (*Biochim. Biophys. Acta*, **1953**, **10**, 613; cf. Stacey, *loc. cit.*).

The polysaccharide was then precipitated twice with ethyl alcohol and isolated by drying from the frozen state. It had $[\alpha]_D$ +60° (equiv., 1030) and contained traces only of nitrogen and phosphorus. Its infrared spectrogram showed peaks at 933 and 837 cm.$^{-1}$, providing evidence of α-(1→6)- and α-(1→4)-linkages (Barker, Bourne, Stacey, and Whiffen, *J.*, **1954**, 171). Its electrophoretic behaviour in the pH range 5·0—8·0 revealed only one component. By acidic hydrolysis with 2N-sulphuric acid at 95°, D-glucose, D-glucuronolactone, D-glucuronic acid, and L-rhamnose were identified on chromatograms as components of the polysaccharide.

Methylation of the Polysaccharide.—(*a*) A solution of the partly purified polysaccharide (10 g.) in water (50 c.c.) was methylated with 30% aqueous sodium hydroxide (300 c.c.) and methyl sulphate (100 c.c.) at 35—42° in the usual manner. Most of the product was isolated by virtue of its insolubility in the hot reaction mixture. The soluble material was recovered from a dialysed solution by concentration to dryness under reduced pressure. In subsequent treatments with these reagents, the partly methylated polysaccharide was kept in solution by the careful addition of acetone. When this was removed by heat, the crude product was precipitated and, after being dried, was purified by extraction with methanol followed by fractional precipitation with ether, and then by precipitation from water with a large excess of acetone. After seven methylations, the hard leathery material (12 g.) was separated into fractions having OMe 33·9—42·2% and ash 10—40%. (*b*) A solution of the partly methylated polysaccharide (21·2 g.; OMe, 37·0%; ash 33·4%) in absolute methanol (700 c.c.) and ether (100 c.c.) was centrifuged to remove inorganic impurities (3·6 g.) and treated with N-sulphuric acid until acid to Congo-red. After removal of a small deposit of sodium sulphate, the acidic polysaccharide (11·9 g.) was precipitated by addition of light petroleum (2 vols.), washed by decantation, and dried. It was then treated in methanol (500 c.c.) with ethereal diazomethane for 36 hr. Removal of the volatile components left a hard grey solid (11·8 g.) (Found: OMe, 38·0; ash, 14·6%). Methylation by both methods was continued until the bulk of the polysaccharide had a methoxyl content of 42·0% and fractional precipitation methods proved it was homogeneous. It was ash-free and had $[\alpha]_D^{18}$ +38° (*c*, 1·0 in MeOH).

Methanolysis of the Methylated Polysaccharide.—The sodium salt (2·2 g.) was heated with 4%

methanolic hydrogen chloride (90 c.c.) in a sealed tube at 100°. After 10 hr. the solution was neutralised with silver carbonate, filtered, and concentrated to a yellow syrup (1·97 g.), n^{19} 1·4650 (Found: OMe, 47·6; ash, 8·4%).

When lower concentrations of methanolic hydrogen chloride were used, scission was incomplete, whereas in 6% concentration, the reagent was too drastic and caused loss of methoxyl.

Hydrolysis of the Mixture of Methylated Glycosides.—The mixture (1·97 g.) was treated with N-sulphuric acid (50 c.c.) at 90°, the optical rotation changing as follows: $[\alpha]_D^{18}$ +34° (initial); +43° (1·5 hr.); +48° (4·5 hr.); +51° (6·5 hr.); +53° (10·5 hr.; equil.).

A syrup (1·8 g.) was isolated by the usual procedure, after the solution had been neutralized with barium carbonate. Separation on a chromatogram using the top layer of 4 : 1 : 5 *n*-butanol–ethanol–water as the mobile phase; and aniline hydrogen phthalate as the indicator showed that at least 4 components were present, *viz.*: N_1, R_F 0·68—0·70, brown spot; N_2, R_F 0·53—0·55, brown spot; U_1, R_F 0·21—0·23 (tailing), red spot; R_F 0·17—0·19 (tailing), red spot.

Separation of the Neutral and Charged Fractions.—(*a*) Amberlite resin IR-100(H) removed barium ions from the hydrolysate, and Deacidite, Amberlite IR-4B, or (most effectively) Amberlite IR-A400 removed hexuronate ions, which were later recovered by elution with aqueous ammonia or barium hydroxide. Thus, a sample (1·80 g.) of the mixed components was separated into a neutral fraction (1·19 g.) and an acidic fraction (0·50 g.) by the agency of Amberlite resins IR-100(H) and IR-A400. (*b*) The syrupy mixture of neutral sugars (0·836 g.) was separated by the method and apparatus described by Hough, Jones, and Wadman (*J.*, 1949, 2511). A 3 : 2 (v/v) mixture of light petroleum (b. p. 40—60°) and *n*-butanol was used as the developing solvent. Two fractions, N1 (0·559 g.) and N2 (0·120 g.) were recovered. The former was a colourless syrup, n^{22} 1·4670, R_G 0·86, $[\alpha]_D^{18}$ +7° (*c*, 1·0 in EtOH), which partially crystallised at 0° and with ether–light petroleum (b. p. 40—60°) gave 2 : 4-*dimethyl*-L-*rhamnose* (0·55 g.), m. p. 91—93° (Found: C, 50·0; H, 8·4; OMe, 32·3. $C_8H_{16}O_5$ requires C, 50·0; H, 8·4; OMe, 32·3%).

Treatment of fraction N1 (0·17 g.) with aniline (0·12 g.) in boiling ethanol (2 c.c.) for 4 hr. and removal of the solvent in a vacuum-desiccator yielded crystalline 2 : 4-*di*-O-*methyl*-N-*phenyl*-L-*rhamnopyranosylamine* (0·08 g., 33%), melting, after crystallisation from ether–light petroleum (b. p. 40—60°), at 141—142·5°, and having $[\alpha]_D^{18}$ +136° ⟶ +4° in 24 hr. (*c*, 0·5 in EtOH) (Found: C, 62·9; H, 7·7; N, 5·3; OMe, 23·1. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9; N, 5·2; OMe, 23·2%).

Further Methylation of Fraction N1.—A single methylation with silver oxide and methyl iodide partially converted 2 : 4-di-*O*-methylrhamnose (0·185 g.) into a crystalline *methyl* 2 : 4-*di*-O-*methyl*-L-*rhamnopyranoside* (20 mg.) which, separated from a syrupy product on a porous tile, had m. p. 98—100°, $[\alpha]_D^{20}$ +85° (*c*, 0·5 in MeOH) (Found: C, 52·1; H, 8·6; OMe, 44·3. $C_9H_{18}O_5$ requires C, 52·4; H, 8·8; 45·3%). After two further methylations of the residue a syrup (0·12 g.) having OMe 55·4% was isolated.

Hydrolysis of the Fully Methylated Glycosides from Fraction N1.—The above syrupy product (0·10 g.) was hydrolysed with 0·5N-sulphuric acid (10 c.c.), $[\alpha]_D$ changing from +53° (initial) to a constant value of +43° in 1 hr., after which the solution was neutralised with barium carbonate and concentrated to dryness and the residue repeatedly extracted with chloroform. Removal of the solvent by distillation left a reducing syrup (70 mg.) with R_G identical with that of 2 : 3 : 4-tri-*O*-methyl-L-rhamnose. The sugar was converted into an aniline derivative by the usual method. After recrystallisation from ethanol–light petroleum (b. p. 60—80°) this melted at 114—116°, alone or in admixture with the authentic aniline derivative of 2 : 3 : 4-tri-*O*-methyl-L-rhamnose.

Examination of Fraction N2.—The syrup (R_G 0·65) (OMe, 26·5%) was fully methylated by methanolic hydrogen chloride followed by silver oxide and methyl iodide. Hydrolysis of the syrupy product with 0·5N-sulphuric acid liberated a reducing sugar with a R_G 1·00. It was converted by aniline into the aniline derivative, m. p. 134°, of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose.

In a separate experiment fraction N2 was shown by the usual method (Smith, *J.*, 1939, 1724) and chromatogaphically to consist largely of 2 : 3 di-*O*-methyl-D-glucopyranose.

Examination of the Barium Salts of the Methylated Uronic Acids.—The residue obtained by concentration of the neutralised eluate from the Amberlite IR-400 column was a yellow, water-soluble powder (0·50 g.) (Found: OMe, 23·0; Ba 23·5. Calc. for $C_9H_{13}O_7\frac{1}{2}Ba$: OMe, 21·4; Ba, 23·7%). Simultaneous esterification and glycoside formation were effected by heating the product (0·5 g.) under reflux with 2% methanolic hydrogen chloride (10 c.c.). A grey precipitate, which rapidly appeared, was filtered off after 12 hr. Distillation of the solvent from

the neutralised filtrate (Ag_2CO_3) left a brown glass (0·257 g.) (Found : OMe, 49·8. Calc. for $C_{10}H_{18}O_7$: OMe, 49·6%).

Treatment of this product with methanolic ammonia for 36 hr. at 0° gave methyl 2 : 3 : 4-tri-*O*-methylglucopyranosiduronamide (12 mg.), m. p. 183°.

A further sample of the main material (0·50 g.) recovered from the methanolic ammonia solution appeared to be an oligosaccharide : it was boiled for 5 hr. with 2N-sulphuric acid. The hydrolysate was neutralised with barium carbonate, and the filtered solution evaporated to dryness. Exhaustive extraction of the barium salt with chloroform gave a syrup (0·11 g.) which was identified chromatographically and by the method of Smith (*loc. cit.*) as 2 : 3-di-*O*-methyl-D-glucopyranose. The barium salts were oxidised as described by Smith (*J.*, 1940, 1035) and Lawson and Stacey (*J.*, 1954, 1925). From the products there was separated 2 : 3 : 4-tri-*O*-methylglucarolactone (0·13 g.), m. p. 107°. The syrupy residue was converted into the amide; 2 : 3-di-*O*-methyl-D-glucarodiamide (0·20 g.), m. p. 156°, crystallised.

The various experiments were repeated in order to get a quantitative assessment of the various substances present. It was estimated that 5·6 g. of methylated polysaccharide contained 2 : 4-di-*O*-methyl-L-rhamnopyranose (3·0 g.), 2 : 3-di-*O*-methyl-D-glucopyranose (0·90 g.), 2 : 3-di-*O*-methyl-D-glucuronic acid (1·95 g.), and 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid (1·05 g.). It is to be noted that these figures indicate more glucuronic acid than was estimated in early analyses, and much less glucose than the 30% indicated by the rhamnose and glucuronic acid estimations. This assessment will need to be repeated with more refined techniques.

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Deoxy-sugars. Part XXVIII. The Stability of Some Substituted Glycosylamines in Aqueous and Non-aqueous Solvents.*

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The chromatographic behaviour of some *N*-substituted D-glycosylamines in aqueous and non-aqueous solvents has been examined. It has been demonstrated that in aqueous solution some hydrolysis of the glycosylamines occurs, and the following equilibrium is set up : *N*-substituted glycosylamine + $H_2O \rightleftharpoons$ (substituted) amine + free sugar. Evidence to support this finding is outlined. The effect of the nature of the amine on the extent of the hydrolysis has been investigated in a preliminary fashion. Comment is made on the effect of this hydrolysis on the changes in optical rotation observed in solutions of these compounds, and the parallel nature of the two changes is noted. Changes in optical rotation of compounds of this class in pyridine are briefly discussed.

As part of a general investigation in this laboratory (cf. Butler, Smith, and Stacey, *J.*, 1949, 3371; Butler, Overend, Smith, and Stacey, *Chem. and Ind.*, 1949, 551; Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433) of the properties of *N*-substituted glycosylamines we have examined their chromatographic behaviour.

On chromatography of aqueous and non-aqueous solutions of 2-deoxy-*N*-*p*-tolyl-D-glucosylamine and -D-galactosylamine, by downward migration on Whatman No. 1 paper

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of the butanol phase of butanol–ethanol–water (5 : 1 : 4) mixture, spots were revealed on development that corresponded in behaviour with the parent 2-deoxyhexoses (*i.e.*, 2-deoxy-D-glucose and 2-deoxy-D-galactose). A similar examination of solutions of *N*-*p*-tolyl-D-galactosylamine showed the presence on the chromatogram of D-galactose (detected by aniline hydrogen phthalate; Partridge, *Nature*, 1949, **164**, 443), together with some of the substituted galactosylamine (detected specifically by the use of *p*-dimethylaminobenzaldehyde; Edward and Waldron, *J.*, 1952, 3631) which had not been hydrolysed. The chromatographic behaviour of these compounds was also examined in anhydrous solvents. No movement of the substances occurred in propylene glycol–toluene (Burton and Zaffaroni, *J. Biol. Chem.*, 1951, **193**, 750; cf. Zaffaroni, Burton, and Keutmann, *Science*, 1950, **111**, 6), benzene–formamide (Burton and Zaffaroni, *loc. cit.*) or anhydrous methanol–heptane (Huelin, *Austral. J. Sci. Res.*, 1952, **5**, *B*, 328). In solvent systems employing methanol, ethanol, propanol, *n*-butanol, and Cellosolve (2-ethoxyethanol) (all anhydrous) either alone or in mixtures, pronounced streaking was encountered. Eventually it was found that the free hexoses could be separated from *N*-arylated hexosylamines by the use of anhydrous Cellosolve–propylene glycol (3 : 1) and, provided that the chromatogram was not overloaded, reasonably discrete spots could be obtained. With this solvent system chromatography of non-aqueous solutions (ethanol and dioxan were used) of the glycosylamines could be effected without significant hydrolysis; only the glycosylamine could be detected on the chromatogram. (In most cases a trace of the free sugar could be detected when the chromatogram was placed in ultraviolet light, but this was attributable to hydrolysis caused by the moisture absorbed during the short periods the chromatograms and materials were unavoidably exposed to the atmosphere.) It was apparent that in the aqueous solvent system initially employed for these experiments the *N*-substituted 2-deoxyhexosylamines had undergone complete hydrolysis, and likewise considerable hydrolysis of *N*-*p*-tolyl-D-galactosylamine had occurred. This was prevented by using a non-aqueous solvent system and in all subsequent chromatographic experiments this was the system adopted.

It is well known that the optical rotation of glycosylamines of this type changes in solution. These rotational changes, particularly those undergone by *N*-substituted D-glucosylamines have been extensively studied (*e.g.*, by Irvine and Gilmour, *J.*, 1908, 1429; Baker, *J.*, 1928, 1583; 1929, 1205; Mitts and Hixon, *J. Amer. Chem. Soc.*, 1944, **66**, 483; Pigman, Cleveland, Couch, and Cleveland, *ibid.*, 1951, **73**, 1976) and in part at least have been attributed to isomerisations, involving interconversions of ring-forms and α- and β-anomers. It is obvious, however, that the marked lability (*i.e.*, hydrolysis) in aqueous solutions of these glycosylamines, as disclosed by our chromatographic experiments, must be borne in mind when considering the changes in optical rotation. Consequently an attempt was made to correlate observations on the extent of the hydrolysis with changes in optical rotation.

The changes in optical rotation of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine under various conditions are shown in Fig. 1. Curves IV and V show the changes in specific rotation of the compound in solution respectively in 50% aqueous ethanol and in water: they are very similar. At equilibrium, chromatography with an anhydrous solvent mixture for irrigation (hence no hydrolysis due to this system) revealed the presence in the solution of non-hydrolysed 2-deoxy-*N*-*p*-tolyl-D-galactosylamine, together with *p*-toluidine and 2-deoxy-D-galactose. That hydrolysis had occurred was confirmed by ethereal extraction of *p*-toluidine from the solution. The presence of unchanged 2-deoxy-*N*-*p*-tolyl-D-galactosylamine on the chromatogram indicated that hydrolysis was not complete. This conclusion was supported by the fact that the final equilibrium value for the optical rotation of the solution did not correspond to the calculated value (based on the measured optical rotation of 2-deoxy-D-galactose in ethanol, and ethanol–water) expected for complete hydrolysis. It is plausible to suggest that the equilibrium shown is set up in aqueous solutions:

$$N\text{-Substituted glycosylamine} + H_2O \rightleftharpoons \text{amine} + \text{free sugar}$$

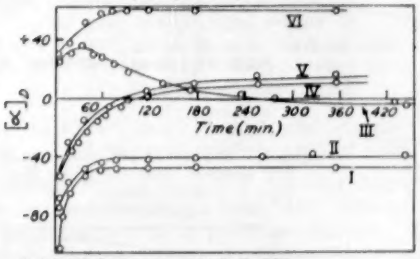
Curve II (Fig. 1) shows the effect of addition of *p*-toluidine (2·5 mols.) on the course of the rotation changes which are normally represented by curve IV: curve II closely parallels

curve I which represents the smaller changes occurring in dry ethanol, when little hydrolysis occurs. Addition of *p*-toluidine favours formation of some of the glycosylamine as would be expected in an equilibrium of the type shown. The reversibility of the changes is also shown by curve III which illustrates the effect of the addition of *p*-toluidine on the course of the mutarotation of 2-deoxy-D-galactose, normally represented by curve VI. Chromatographic examination at the equilibrium state of the solution used to obtain curve III showed the presence in the liquid of some 2-deoxy-*N*-*p*-tolyl-D-galactosylamine, obviously formed by interaction of the sugar and the base.

Comparison of the results depicted in Figs. 1 and 2 (the latter shows results obtained with *N*-*p*-tolyl-D-galactosylamine) indicates the influence of the 2-deoxy-group on the glycosidic centre in the galactose series. Whereas equilibrium of *N*-*p*-tolyl-D-galactosylamine in aqueous solution is attained in approximately 60 hours (Fig. 2, curve IV), the comparable equilibrium of the 2-deoxy-analogue is complete within 5 hours (Fig. 1, curve V).

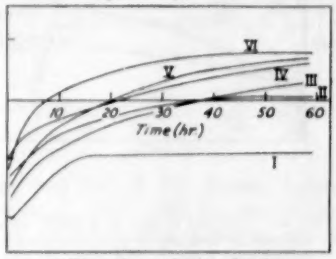
In addition to depicting changes with *N*-*p*-tolyl-D-galactosylamine, Fig. 2 shows the corresponding results obtained with *N*-phenyl-D-galactosylamine. In our experience

FIG. 1. *Optical rotation changes of 2-deoxy-N-p-tolyl-D-galactosylamine.*



I, 1% *Solution in anhyd.* EtOH.
II, 1% *Solution in* 50% *aq.* EtOH + p-*toluidine* (2·5 *mols.*).
III, 1% *Solution of 2-deoxy-D-galactose in* 50% *aq.* EtOH + p-*toluidine* (1%).
IV, 1% *Solution in* 50% *aq.* EtOH.
V, 1% *Solution in* H_2O.
VI, 1% *Solution of 2-deoxy-D-galactose in* 50% *aq.* EtOH.

FIG. 2. *Optical rotational changes of N-galactostylamines.*



N-Phenyl-D-galactosylamine.
I, 0·4% *in anhyd.* EtOH.
III, 1·0% *in* 50% *aq.* EtOH.
V, 1·0% *in* H_2O.

N-*p*-Tolyl-D-galactosylamine.
II, 1·0% *in* 80% *aq.* EtOH.
IV, 1·0% *in* H_2O.
VI, 0·5% *in* 50% *aq.* EtOH.

N-*p*-tolyl-D-galactosylamine was not appreciably soluble in anhydrous ethanol and a 0·2% solution could not be obtained. Likewise the 0·4% solution of *N*-phenyl-D-galactosylamine in this solvent was obtained only with much difficulty, but dissolution of these compounds occurred more readily if traces of water were added to the ethanol. The different amine moieties did not materially affect the overall rates of equilibration, although the initial rate of change of the derivative of *p*-toluidine was greater than for the aniline derivative (Fig. 2, curves IV and V respectively). An attempt to determine the effect of basic strength of the amine on the changes was not very successful. In addition to the derivatives of D-galactose with aniline (pK $5{\cdot}3 \times 10^{-10}$) and *p*-toluidine (p$K$ $1{\cdot}5 \times 10^{-9}$), a derivative was made from this sugar and *p*-nitroaniline (pK $1{\cdot}2 \times 10^{-13}$). However, *N*-*p*-nitrophenyl-D-galactosylamine was practically insoluble in water and ethanol. In a saturated aqueous solution no hydrolysis could be detected chromatographically. The substance dissolved in pyridine to give a solution of constant specific rotation. Apparently the weakly basic amines form more stable *N*-glycosides. It is interesting that the absence of hydrolysis is accompanied by a corresponding absence of rotation changes (*i.e.*, no " mutarotation ").

In an equilibrium of the type shown, the hydrolysis of the glycosylamine will result in a pH change in the system. The dependence of the rate of the rotational changes on the pH of the solution is clearly shown in Fig. 3 in which the rotation changes are recorded of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine in various buffered aqueous solutions. Increase in

pH considerably retards the changes, and decrease accelerates them. Comparable results were obtained with the analogous derivative of D-galactose: the rates were much more rapid with the derivative of the 2-deoxy-sugar. Hence, although derivatives of the more basic amines are less stable than those derived from weaker amines, the rate of hydrolysis of the former sugar–base compounds will eventually become very slow owing to the competitive retarding influence of the higher pH developed as hydrolysis proceeds. That an increase in pH occurs in an aqueous solution of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine is evident from the results recorded in Fig. 4. It will be seen that the course of this pH change closely corresponds to that in optical rotation shown in Fig. 1. Fig. 5 shows the corresponding values obtained for pH changes with time of aqueous solutions of *N*-*p*-tolyl- and *N*-phenyl-D-galactosylamine. The measurable increase in the pH of these solutions provides a method of estimating the degree of hydrolysis that has occurred and the extent to which this is responsible for the changes in optical rotation. By comparing the maximum

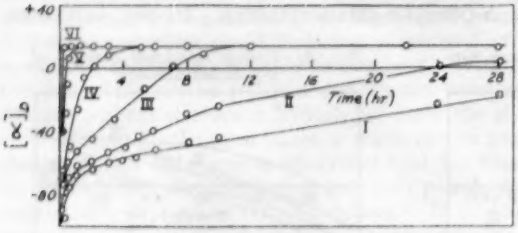


FIG. 3. *Optical rotational changes of* 2-*deoxy*-N-*p*-*tolyl*-D-*galactosylamine* (1%) *in various buffer solutions.*

Curve	I	II	III	IV	V	VI
pH ...	9·98	9·08	8·59	7·82	7·00	6·00

FIG. 4. *Increase in* pH *of a* 1·0% *aqueous solution of* 2-*deoxy*-N-*p*-*tolyl*-D-*galactosylamine with time.*

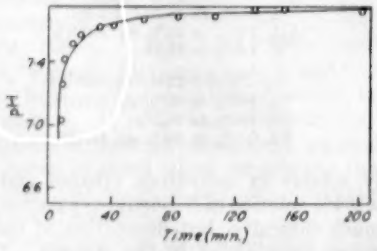
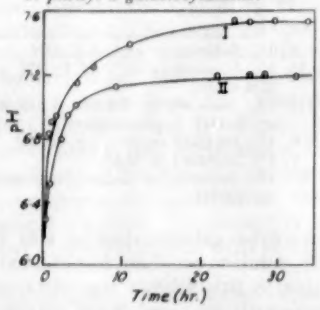


FIG. 5. *Increase in* pH *with time of* 1% *aqueous solutions of* (I) N-*p*-*tolyl*-D-*galactosylamine, and* (II) N-*phenyl*-D-*galactosylamine.*



pH value attained by a solution of the glycosylamine with that developed by a known concentration of the free base in the same solvent, an estimate of the extent of hydrolysis can be obtained. This method of estimation would not upset equilibrium conditions [previous methods that have been used to determine the extent of the hydrolysis of *N*-substituted D-glucosylamines include extraction of the free base (Mitts and Hixon, *loc. cit.*; Pigman *et al.*, *loc. cit.*), estimations based on the Van Slyke method (Pigman *et al.*, *loc. cit.*), and potentiometric titration of the free base in solution (Mitts and Hixon, *loc. cit.*)]. Since primary amines in solution readily absorb carbon dioxide from the atmosphere (Akashi, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, **1933**, **20**, Nos. 411—413) it is necessary to measure the pH with nitrogen sweeping over the surface of the liquid if reproducible results are required.

Calculations based on results in Figs. 1 and 5, and a calibration graph of the change of pH with concentration of *p*-toluidine in water, gave comparable figures of 87% and 80·5% hydrolysis based on optical rotation and pH measurements respectively for equilibrated solutions of *N*-*p*-tolyl-D-galactosylamine in water. So in this case hydrolysis could account almost entirely for the observed changes in optical rotation.

The preceding facts (cf. Barclay, Foster, and Overend, *Chem. and Ind.*, 1953, 462) emphasize the care needed in attributing the changes in optical rotation of solutions of *N*-substituted glycosylamines to true mutarotational phenomena (cf. Irvine and Gilmour, *J.*, 1908, 1429; Irvine and McNicoll, *J.*, 1910, 1449; Kuhn and Dansi, *Ber.*, 1936, **69**, 1745; Weygand, *Ber.*, 1939, **72**, 1663) without prior ascertainment of the effect on the compounds of water and pH changes.

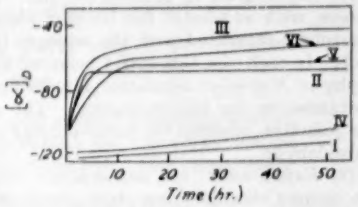
The present results confirm the behaviour of glycosylamines described by previous authors (cf. Mitts and Hixon *loc. cit.*; Pigman *et al.*, *loc. cit.*) and extend the range of generalisations to include derivatives of 2-deoxy-sugars.

As there are conflicting reports on the changes in optical rotation occurring in solutions of glycosylamines in pyridine, we have re-examined the optical rotational behaviour of some derivatives of this type in this solvent. Since we considered that the presence of traces of moisture might account for the differences, great care was taken to exclude moisture, in the compounds and in the solvent and during the experiment. It was then found that neither *N*-phenyl-D-galactosylamine nor *N*-*p*-tolyl-D-galactosylamine underwent any

FIG. 6. *Optical rotational changes of* N-*galactosylamines.*

N-*p*-Tolyl-D-galactosylamine.
I, 1·0% *in dry pyridine.*
II, 1·0% *in dry pyridine* (+5% *of water*).
III, 1·0% *in dry pyridine* (+10% *of water*).

N-Phenyl-D-galactosylamine
IV, 1·0% *in dry pyridine.*
V, 1·0% *in dry pyridine* (+5% *of water*).
VI, 1·0% *in dry pyridine* (+10% *of water*).



significant change in optical rotation during 40 hours (see Fig. 6) (cf. Butler, Laland, Overend, and Stacey, *J.*, 1950, **1433**; Ellis and Honeyman, *J.*, 1952, 1490, for observations on these compounds in pyridine solution). Addition of water resulted, however, in considerable changes in optical rotation (Fig. 6, curves II, III, V, and VI).

EXPERIMENTAL

2-Deoxy-N-p-tolyl-D-glucosylamine.—2-Deoxy-D-glucose (0·6 g.) and *p*-toluidine (0·6 g.) were heated together at 95° for 1 hr. After cooling, the solid melt was extracted with ether to remove excess of *p*-toluidine, and the residue recrystallised from a large volume of absolute ethanol. 2-Deoxy-*N*-*p*-tolyl-D-glucosylamine (0·65 g., 69%) was obtained as colourless needles, m. p. 192° (Found: C, 61·75; H, 7·5; N, 5·7. Calc. for $C_{13}H_{19}O_4N$: C, 61·7; H, 7·5; N, 5·5%). Kuhn and Dansi, (*Ber.*, 1936, **69**, 1745) report m. p. 192° for this compound.

2-Deoxy-*N*-*p*-tolyl-D-galactosylamine, prepared similarly (77% yield) from 2-deoxy-D-galactose, had m. p. 143° (from ethanol) and $[\alpha]_D^{20}$ − 44° (equil.) (*c*, 1·0 in EtOH) (Found: C, 61·7; H, 7·5; N, 5·7%).

N-Aryl Derivatives of D-Galactosylamine.—(a) *N-Phenyl derivative.* D-Galactose (2·5 g.), aniline (2 g.), and water (0·75 ml.) were heated at 80° for 15 min. and then stirred with absolute ethanol (5 ml.). The solid that separated was recrystallised from ethanol and afforded pure *N*-phenyl-D-galactosylamine (2·7 g., 76%), m. p. 149° (decomp.), $[\alpha]_D^{18}$ − 118° (*c*, 1·0 in dry pyridine) (Found: C, 56·8; H, 6·7; N, 5·5. Calc. for $C_{12}H_{17}O_5N$: C, 56·5; H, 6·7; N, 5·5%). Weygand (*Ber.*, 1939, **72**, 1663) reports m. p. 144°.

(b) N-p-*Tolyl derivative.* D-Galactose (2 g.), *p*-toluidine (1·6 g.), and water (0·6 ml.) were mixed together at 80°. After 10 min. the mixture was homogeneous: heating was continued for a further 15 min. and then the product (2·8 g., 85%) was isolated as described above. It had m. p. 154—156° (decomp.) and $[\alpha]_D^{18}$ − 122° (*c*, 1·0 in dry pyridine) (Found: C, 57·9; H, 7·0; N, 5·2. Calc. for $C_{13}H_{19}O_5N$: C, 58·0; H, 7·1; N, 5·2%). Weygand (*loc. cit.*) reports m. p. 154—155°.

(c) N-p-*Nitrophenyl derivative.* D-Galactose (2 g.) and *p*-nitroaniline (2 g.) were dissolved in methanol (40 ml.), and concentrated hydrochloric acid (0·08 ml.) was added. The solution was heated under reflux for 2 hr. and the crystalline product was filtered off and washed with ether. *N*-*p*-Nitrophenyl-D-galactosylamine (2·5 g., 75%) was obtained as yellow needles, which after recrystallisation from 80% aqueous ethanol had m. p. 218—219° (decomp.) and $[\alpha]_D^{20}$ − 209° (*c*, 1·0 in pyridine) (Found: C, 48·3; H, 5·2; N, 9·35. Calc. for $C_{12}H_{14}O_7N_2$: C, 48·0;

H, 5·4; N, 9·3%). Frérejacque (*Compt. rend.*, 1938, **207**, 638) reports m. p. 203° and $[\alpha]_D^{20}$ — 202° (in pyridine).

Chromatography Experiments with the N-Glycosides.—Downward migration on Whatman No. 1 filter paper was used throughout. Solutions of the *N*-glycosides were as follows: (*a*) Saturated solution of 2-deoxy-*N*-*p*-tolyl-D-glucosylamine in (i) anhydrous ethanol, (ii) aqueous ethanol, (iii) water, and (iv) anhydrous dioxan; (*b*) 1% solutions of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine in (i) anhydrous ethanol, (ii) aqueous ethanol, and (iii) water; (*c*) a saturated solution of *N*-*p*-tolyl-D-galactosylamine in absolute ethanol and 1% solutions of this compound in aqueous ethanol and in water.

Free reducing sugars and their *N*-glycosides were detected on chromatograms by spraying with aniline hydrogen phthalate reagent and developing at 100° for 3 min. The *N*-glycosides and the free amines were detected specifically by spraying the chromatograms with a solution of *p*-dimethylaminobenzaldehyde [1% in ethanol, diluted (4 : 1) with concentrated hydrochloric acid before use] and development at 80° for 1 min. With this reagent the *N*-glycosides and amines gave a bright yellow complex, whereas the 2-deoxy-D-hexoses gave a grey colour. The normal hexoses were not revealed by this reagent.

(1) *Experiments in aqueous solvents.* Chromatography of the *N*-glycosides of the 2-deoxyhexoses, with as solvent the butanol phase of butanol–ethanol–water (5 : 1 : 4, v/v) and in an atmosphere saturated with the aqueous phase of this mixture, gave a single spot on development. In each case this entity behaved identically with the parent 2-deoxyhexose. Chromatography of *N*-*p*-tolyl-D-galactosylamine under the same conditions showed the presence of two substances on the chromatogram. The slower-moving material behaved in identical fashion to D-galactose, whereas the faster-moving spot gave a bright yellow colour with *p*-dimethylaminobenzaldehyde.

(2) *Experiments in non-aqueous solvents.* The chromatograms were irrigated with anhydrous Cellosolve–propylene glycol (3 : 1, v/v) in an atmosphere saturated with the same mixture. With anhydrous solutions the chromatograms revealed the presence of only one material in each case, which gave a yellow colour with *p*-dimethylaminobenzaldehyde. The R_F values differed from those of the free sugars. Occasionally slight traces of spots having R_F values identical with those of the free sugars were detected in ultraviolet light.

Mutarotational Studies on the Substituted Glycosylamines and their 2-Deoxy-analogues.—The solutions listed in Figs. 1—3 and 6 were used for the mutarotational studies. The pyridine used was distilled six times from phosphoric oxide and was stored in a sealed container. Polarimetric observations on dry pyridine solutions were carried out in a sealed polarimeter tube. The 1% solution of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine in anhydrous ethanol was prepared by heating the mixture for 10 min. Likewise it was necessary to heat *N*-phenyl-D-galactosylamine in anhydrous ethanol for 30 min. in order to obtain a 0·4% solution. *N*-*p*-Tolyl-D-galactosylamine was practically insoluble in anhydrous ethanol even warm.

The buffers employed were:

M/15-Na_2HPO_4–M/15-KH_2PO_4 ...	pH 6·0	M/8-Barbituric acid–sodium barbiturate	pH 8·59
,, ,, ...	pH 7·0	M/10-$NaHCO_3$–M/10-Na_2CO_3	pH 9·08
,, ,, ...	pH 7·82	,, ,, ...	pH 9·98

The solutions studied for mutarotation were also examined by filter-paper chromatography with anhydrous Cellosolve–propylene glycol (3 : 1, v/v). Aqueous solutions of the N-glycosides gave in each case two spots on the chromatogram. The slower-moving spot behaved as the free sugar and the faster-moving spot gave a bright yellow colour with *p*-dimethylaminobenzaldehyde. Non-aqueous solutions showed only the faster-moving spot, although a trace of the slower-moving material was visible in ultraviolet light.

Measurement of pH *Changes.*—A standard Cambridge pH meter was used. The pH changes of 1% solutions in water of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine, *N*-*p*-tolyl-D-galactosylamine, and *N*-phenyl-D-galactosylamine were noted at intervals (see Fig. 4). The increase in pH with increase in concentration of *p*-toluidine in water was also recorded. Values obtained were:

Concn. in H_2O of *p*-toluidine (%)	0·05	0·1	0·2	0·3	0·35	0·4	0·45	0·5
pH	6·82	7·05	7·35	7·54	7·61	7·65	7·70	7·72

Isolation of p-*Toluidine from an Aqueous-ethanolic Solution of 2-Deoxy-*N-p-*tolyl-*D-*galactosylamine.*—After a solution of 2-deoxy-*N*-*p*-tolyl-D-galactosylamine in 50% aqueous ethanol (1% solution in 250 ml.) had been allowed to equilibrate (as shown by the specific rotation) it was diluted with water to 500 ml. and extracted with ether (4 × 50 ml.). The ethereal extract

was dried (Na_2SO_4) and evaporated to dryness. The residue was redissolved in ether, and the solution washed with water, dried, and evaporated. The solid residue (96 mg.) had m. p. 40—42° alone or on admixture with *p*-toluidine. It readily afforded a toluene-*p*-sulphonyl derivative, m. p. and mixed m. p. 116—117° (Muller and Weisenger, *Ber.*, 1879, **12**, 1348, report m. p. 117°).

The aqueous layer remaining after the initial ether-extraction was examined chromatographically [Cellosolve–propylene glycol, (3 : 1)] and the presence in solution of 2-deoxy-D-galactose was demonstrated.

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*Methyl-substituted αβ-Unsaturated Acids. Part II.**

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In connection with studies of mycolipenic acid several long-chain methyl-substituted αβ-unsaturated acids have been prepared and converted, *via* the amides and dimethylamides, into the amines and dimethylamines, respectively.

IN previous communications (Bailey, Polgar, and Robinson, *J.*, 1953, 3031; Polgar, *J.*, 1954, 1008) mycolipenic acid, from the lipids of tubercle bacilli, was shown to be (+)-2 : 4 : 6-trimethyltetracos-2-enoic acid. It was of interest to study the effect of modifications in the structural features of this acid on the biological activity, and the present paper describes syntheses of 2-methyloctadec-2-enoic (I; $n = 14$), 2-methyleicos-2-enoic (I; $n = 16$), 2 : 4-dimethyleicos-2-enoic (II; $n = 15$), and 2 : 4-dimethyldocos-2-enoic acid (II; $n = 17$). The acids were obtained from the corresponding saturated acids by α-bromination, followed by reaction with methanol and dehydrobromination of the resulting bromo-ester by means of pyridine according to the procedure given in Part I.* Of the requisite saturated acids, the preparations of 2-methyleicosanoic and 2 : 4-dimethyldocosanoic acid have already been reported (Bailey, Polgar, and Robinson, *loc. cit.*), and 2-methyloctadecanoic and 2 : 4-dimethyleicosanoic acid were obtained by analogous procedures.

(I) $CH_3{\cdot}[CH_2]_n{\cdot}CH{:}CMe{\cdot}CO_2H$ $CH_3{\cdot}[CH_2]_n{\cdot}CHMe{\cdot}CH{:}CMe{\cdot}CO_2H$ (II)

It has been shown in Part I* that dehydrobromination of methyl (—)-2-bromo-2 : 4 : 8-trimethylnonanoate (optically active in respect of $C_{(4)}$) by pyridine, followed by hydrolysis of the resulting unsaturated ester, gave an optically active acid which, judged by its extinction coefficient in the ultraviolet, appeared to be essentially αβ-unsaturated. The formation of a βγ-ethylenic linkage would result in the loss of the original asymmetric centre at $C_{(4)}$. Since a βγ-unsaturated acid is more readily esterified than the αβ-unsaturated isomer (cf. Sudborough and Thomas, *J.*, 1911, **99**, 2307), we have submitted a specimen of the above optically active acid to partial esterification with a view to examine the optical rotation of the remaining acidic fraction. The latter exhibited the same rotatory power as the initial product, thus indicating that the pyridine dehydrobromination yielded only the αβ-unsaturated isomer. In comparative studies with the bromo-ester from 2-methyloctadecanoic acid, pyridine dehydrobromination, followed by hydrolysis of the resulting unsaturated ester, gave 2-methyloctadec-2-enoic acid (I; $n = 14$), m. p. 64° (log $\varepsilon_{max.}$ 4·11 at 2160 Å), whereas dehydrobromination by means of quinoline yielded the acid with a somewhat lower m. p. of 63·5° (log $\varepsilon_{max.}$ 4·07 at 2160 Å), and diethylaniline dehydrobromination gave an acid having m. p. 58° (log $\varepsilon_{max.}$ 3·90 at 2180 Å) which, thus, appeared only partly αβ-unsaturated. Therefore, pyridine seemed the most satisfactory of the organic

* Part I, *J.*, 1953, 132.

bases employed. Some dehydrobrominations involving the action of ethanolic potassium hydroxide are included in the Experimental section.

It was of interest to examine the physiological properties of water-soluble derivatives of the synthetic acids. For comparative studies 2-methyleicos-2-enoic, 2 : 4-dimethyldocos-2-enoic, and the corresponding saturated acids were converted into the amides and dimethylamides which, on reduction with lithium aluminium hydride, afforded the corresponding amines. It has been reported (Uffer and Schlittler, *Helv. Chim. Acta*, 1948, **31**, 1397) that α-ethylcrotonamide on treatment with lithium aluminium hydride for 20 hr. yields the corresponding saturated amine. However, in the present work refluxing ethereal solutions of the αβ-unsaturated amides with lithium aluminium hydride for periods not exceeding 2 hr. (Brown, " Organic Reactions," John Wiley & Sons, Inc., New York, 1951, Vol. VI, p. 469; Micovic and Mihailovic, *J. Org. Chem.*, 1953, **18**, 1190) did not appear to affect the double bond.

The physiological studies were carried out by Dr. J. Ungar of Glaxo Laboratories Ltd. On intraperitoneal injection into guinea pigs, 2-methyloctadec-2-enoic acid (I; $n = 14$) produced discrete nodules of cheesy consistency in the organs of the peritoneal cavity; the effects were transitory. 2 : 4-Dimethyleicos-2-enoic acid (II; $n = 15$) acted as a non-specific irritant. 2 : 4-Dimethyldocos-2-enoic acid (II; $n = 17$) showed very low activity in producing a non-specific reaction.

Of the unsaturated amines, the hydrochlorides of 2-methyleicos-2-enylamine (III) and 2 : 4-dimethyldocos-2-enylamine (V) were very active in producing lesions of the granulomatous type in abdominal organs with marked lymphatic spread. 2-Methyleicos-2-enyldimethylamine hydrochloride (IV) was only an irritant, and 2 : 4-dimethyldocos-2-enyldimethylamine hydrochloride (VI) was inactive.

(III) $CH_3 \cdot [CH_2]_{14} \cdot CH{:}CMe \cdot CH_2 \cdot NH_2,HCl$ $CH_3 \cdot [CH_2]_{17} \cdot CHMe \cdot CH{:}CMe \cdot CH_2 \cdot NH_2,HCl$ (V)

(IV) $CH_3 \cdot [CH_2]_{14} \cdot CH{:}CMe \cdot CH_2 \cdot NMe_2,HCl$ $CH_3 \cdot [CH_2]_{17} \cdot CHMe \cdot CH{:}CMe \cdot CH_2 \cdot NMe_2,HCl$ (VI)

The hydrochlorides of the saturated amines corresponding to (III)—(VI) were all active.

Experimental

The absorption spectra were measured by Mr. F. Hastings and Dr. F. B. Strauss. Ultraviolet spectra were determined in methanol.

Partial Esterification of (−)-2 : 4 : 8-*Trimethylnon-2-enoic Acid.*—For the preparation of the acid the procedure described in Part I (*loc. cit.*) was employed, except that the starting material, (+)-citronellal, was purified by Tiemann's procedure (*Ber.*, 1899, **32**, 812), and the intermediate bromo-ester, *methyl* (−)-2-*bromo*-2 : 4 : 8-*trimethylnonanoate* was isolated by distillation. It had b. p. 136—139°/9 mm., $[\alpha]_D^{16}$ −6·7° (homog.), d_4^{16} 1·139, n_D^{19} 1·4627 (Found : C, 53·0; H, 8·4; Br, 27·2. $C_{13}H_{25}O_2Br$ requires C, 53·2; H, 8·5; Br, 27·3%), and gave on pyridine dehydrobromination, followed by hydrolysis of the resulting unsaturated ester, (−)-2 : 4 : 8-trimethylnon-2-enoic acid (Found : C, 72·9; H, 11·2. Calc. for $C_{12}H_{22}O_2$: C, 72·7; H, 11·1%) having $[\alpha]_D^{17}$ −25·6° (*c*, 10·07 in ether; *l*, 0·5), a slightly higher value than that previously found (*loc. cit.*). The acid (2·7 g.) was kept with 5% (w/v) methanolic sulphuric acid (30 c.c.) at the room temperature for 0·5 hr. The mixture was then diluted with water and extracted with ether from which the acidic fraction was removed with 5% aqueous potassium carbonate. Acidification of the alkaline extract and ether-extraction, followed by distillation, gave the unesterified portion of the original acid (2 g.), $[\alpha]_D^{14}$ −25·8° (*c*, 9·99 in ether; *l*, 0·5). The recovered acid (1 g.) was refluxed with 2·5% (w/v) methanolic sulphuric acid (30 c.c.) for 8 min., and the acidic product separated from the ester fraction (0·21 g.) as above. The acid had $[\alpha]_D^{15}$ −25·7° (*c*, 10·20 in ether; *l*, 0·5).

2-*Methyloctadec-2-enoic Acid* (I; $n = 14$).—2-Methyloctadecanoic acid was obtained essentially as described previously for the preparation of 2-methyleicosanoic acid (Bailey, Polgar, and Robinson, *loc. cit.*). Hexadecan-1-ol (97 g.; b. p. 166°/2 mm.) was converted by reaction with iodine (52 g.) and red phosphorus (5 g.) into the iodide (122·5 g.), b. p. 206—207°/10 mm., which was condensed with the sodio-derivative of ethyl methylmalonate (from 8·4 g. of sodium, 66 g. of ethyl methylmalonate, and 205 c.c. of ethanol), the mixture being heated under reflux for 9 hr. The usual successive stages (hydrolysis, decarboxylation) afforded the acid (80 g.), b. p. 200—201°/2 mm., m. p. 55° (Found : C, 76·0; H, 12·7. Calc. for $C_{19}H_{36}O_2$: C, 76·5; H, 12·8%).

Its amide, after crystallisation from ethanol, had m. p. 105° (Found : C, 76·1; H, 13·1; N, 4·9. Calc. for $C_{19}H_{39}ON$: C, 76·6; H, 13·2; N, 4·7%). The *p-bromophenacyl ester*, crystallised from ethanol–methanol, had m. p. 83—83·5° (Found : C, 65·3; H, 8·8; Br, 16·4. $C_{27}H_{43}O_3Br$ requires C, 65·5; H, 8·7; Br, 16·1%). Schneider and Spielman (*J. Biol. Chem.*, 1942, **142**, 345) give m. p. 54·55° for the acid, and m. p. 104·5° for the amide.

The preceding acid (50 g.) was heated with bromine (98 g.) in the presence of red phosphorus (5·2 g.) for 7·5 hr., as already described for similar cases (Part I, *loc. cit.*), and the resulting crude acid bromide converted, by means of methanol (50 c.c.), into *methyl 2-bromo-2-methyloctadecanoate* (55·7 g.), b. p. 190—192°/0·5 mm., n_D^{19} 1·4656 (Found : C, 61·9; H, 9·9; Br, 20·2. $C_{20}H_{39}O_2Br$ requires C, 61·4; H, 10·0; Br, 20·45%).

A 7-g. portion of this bromo-ester was refluxed with anhydrous pyridine (33 g.) for 19 hr. *Methyl 2-methyloctadec-2-enoate* was obtained as an oil (4·4 g.), b. p. 159—163°/0·2 mm., n_D^{17} 1·4599, log $\varepsilon_{max.}$ 4·08 at 2180 Å (Found : C, 77·7; H, 12·3. $C_{20}H_{38}O_2$ requires C, 77·4; H, 12·3%). The corresponding *acid*, obtained by refluxing the unsaturated ester (3·2 g.) with a solution of potassium hydroxide (2 g.) in ethanol (30 c.c.) and water (5 c.c.) for 75 min., distilled at 195—197°/0·35 mm. (2·8 g.) and had m. p. 64° (Found : C, 77·4, H, 12·5. $C_{19}H_{36}O_2$ requires C, 77·0; H, 12·3%). Ultraviolet absorption : log $\varepsilon_{max.}$ 4·11 at 2160 Å. Infrared absorption : 1647 and 1697 cm.$^{-1}$ (–C:C–C:O). The *amide*, after crystallisation from ethanol, had m. p. 82° (Found : C, 77·0; H, 12·2; N, 4·5. $C_{19}H_{37}ON$ requires C, 77·3; H, 12·5; N, 4·7%).

When the above bromo-ester (7 g.) was heated with pyridine (26·5 g.) on a steam-bath for 6 hr., and kept at the room temperature for another 36 hr., the product was found on analysis to contain considerable amounts of bromine (Found : C, 64·0; H, 10·5; Br, 15·7%).

Comparative Dehydrobromination Experiments.—(i) Methyl 2-bromo-2-methyloctadecanoate (7 g.) and quinoline (25 g.; freshly distilled over potassium hydroxide) were gently refluxed for 0·5 hr. After dilution with water, the product was collected with ether, and distilled in steam until free from quinoline. The residue, isolated with the aid of ether, had been partly hydrolysed to the acid. It was refluxed with potassium hydroxide (3 g.) in ethanol (50 c.c.) and water (7 c.c.) for 2 hr., and the product worked up in the usual manner. Distillation afforded 2-methyloctadec-2-enoic acid (4·7 g.), log $\varepsilon_{max.}$ 4·07 at 2160 Å, m. p. 63·5° after crystallisation from methanol (Found : C, 77·2; H, 12·1%).

(ii) The above bromo-ester (7 g.) was refluxed with diethylaniline (25 g.; freshly distilled over potassium hydroxide) for 2 hr., and then added to 10% hydrochloric acid (300 c.c.). The product was isolated by means of ether and freed from diethylaniline by washing with 10% hydrochloric acid, and then with water. Distillation gave the unsaturated ester (4·1 g.), b. p. 155—161°/0·15 mm., n_D^{17} 1·4569, log $\varepsilon_{max.}$ 3·93 at 2180 Å (Found : C, 77·1; H, 12·6%). The corresponding acid, obtained by refluxing the ester with 5% ethanolic potassium hydroxide for 1·5 hr., and isolated by distillation, had m. p. 58° (Found : C, 77·4; H, 12·2%). It exhibited log $\varepsilon_{max.}$ 3·90 at 2180 Å, and its infrared spectrum showed absorption bands at 1647 and 1697 cm.$^{-1}$ with an inflection at 1718 cm.$^{-1}$.

(iii) The bromo-ester (8 g.) was added to a solution of potassium hydroxide (8 g.) in ethanol (36 c.c.) and water (4 c.c.), and the mixture kept at the room temperature for 20 hr. The solution, containing a voluminous precipitate of potassium bromide, was diluted with water, acidified (10% hydrochloric acid), and extracted with ether. The product (5·7 g.), b. p. 180—195°/0·07 mm., was a wax-like solid, m. p. 44—48° (Found : C, 75·1; H, 12·1%), log $\varepsilon_{max.}$ 3·71 at 2140 Å, representing a mixture of unsaturated acids and the α-hydroxy-acid. Accordingly, it gave on oxidation with lead tetra-acetate octadecan-2-one, isolated as its semicarbazone, m. p. 125·5—126° after crystallisation from ethanol (Found : C, 70·4; H, 12·1; N, 12·7. Calc. for $C_{19}H_{39}ON_3$: C, 70·15; H, 12·0; N, 12·9%).

(iv) A solution of methyl (–)-2-bromo-2 : 4 : 8-trimethylnonanoate (4 g.) and potassium hydroxide (4 g.) in ethanol (18 c.c.) and water (2 c.c.) was kept at the room temperature for 18 hr. (within a few minutes there was a considerable precipitate of potassium bromide). Acidification with 5% hydrochloric acid, followed by extraction with ether and distillation, gave a product (2·7 g.), b. p. 150—165°/14 mm., which had no measurable rotation (c, 54 in ether; l, 0·5). Light absorption : log $\varepsilon_{max.}$ 3·66 at 2100 Å. It was chromatographed in light petroleum (b. p. 40—60°; 100 c.c.) on a silica column (35 × 1 cm.), prepared in the same solvent. Two main fractions were obtained; the first (0·8 g.) was eluted by light petroleum, and the second (0·7 g.) by methanol–benzene (1 : 10). The former, a mixture of unsaturated acids, distilled at 165°(bath)/12 mm. as an oil (Found : C, 72·6; H, 11·2. Calc. for $C_{12}H_{22}O_2$: C, 72·7; H, 11·1%), light absorption : log $\varepsilon_{max.}$ 3·88 at 2140 Å, and had no rotation in ethereal solution. The second fraction, a wax-like solid, was a hydroxy-acid [Found : active hydrogen

(Zerewitinoff), 0·8. Calc. for $C_{13}H_{24}O_3$: 0·9%]. It showed no high-intensity absorption in the ultraviolet (2050—2400 Å).

2-Methyleicos-2-enoic Acid (I; $n = 16$).—2-Methyleicosanoic acid (20 g.; Bailey, Polgar, and Robinson, *loc. cit.*) was heated with bromine (30 g.) in the presence of red phosphorus (1·61 g.) for 8 hr. in the manner already described. Next day anhydrous methanol (100 c.c.) was added, and the mixture refluxed for 3 hr. The crude bromo-ester was then refluxed with pyridine (100 c.c.) for 16 hr. and the resulting mixture poured into dilute hydrochloric acid. Isolation with ether gave *methyl 2-methyleicos-2-enoate* (16 g., 77%) as a colourless liquid, b. p. 172°/0·08 mm. (Found: C, 77·8; H, 12·5. $C_{22}H_{42}O_2$ requires C, 78·2; H, 12·4%). This was refluxed with a solution of potassium hydroxide (6 g.) in water (30 c.c.) and ethanol (60 c.c.) for 5 hr. On cooling, the potassium salt of the acid separated and was collected. It was then dissolved in hot water, and the solution acidified with hydrochloric acid, yielding *2-methyleicos-2-enoic acid* which crystallised from ethanol in fine needles, m. p. 70—70·8° (Found: C, 77·3; H, 12·2. $C_{21}H_{40}O_2$ requires C, 77·8; H, 12·4%). Light absorption: $\log \varepsilon_{max.}$ 4·13 at 2180 Å. The *amide*, prepared *via* the acid chloride (obtained by means of purified thionyl chloride) in the usual manner, had m. p. 88—88·5° (Found: C, 78·2; H, 12·7; N, 4·2. $C_{21}H_{41}ON$ requires C, 78·0; H, 12·7; N, 4·3%). The *dimethylamide*, obtained from the acid chloride by reaction with 33% aqueous dimethylamine, distilled at 203—210°(bath)/0·04 mm., and had m. p. 27—27·5° (Found: C, 78·0; H, 12·6; N, 4·2. $C_{23}H_{45}ON$ requires C, 78·6; H, 12·9; N, 4·0%).

The corresponding saturated acid, 2-methyleicosanoic acid (see above), gave an amide, m. p. 107—107·5° (from ethanol) (Found: C, 77·8; H, 13·2; N, 4·2. Calc. for $C_{21}H_{43}ON$: C, 77·5; H, 13·2; N, 4·3%). Its *dimethylamide* crystallised from methanol in fine needles, m. p. 56—57° (Found: C, 78·0; H, 13·2; N, 4·1. $C_{23}H_{47}ON$ requires C, 78·1; H, 13·3; N, 4·0%).

2 : 4-Dimethyleicos-2-enoic Acid (II; $n = 15$).—*2 : 4-Dimethyleicosanoic acid* was prepared from 2-methyloctadecanoic acid as described for the preparation of 2 : 4-dimethyldocosanoic acid (Bailey, Polgar, and Robinson, *loc. cit.*). The intermediate, *2-methyloctadecan-1-ol*, b. p. 163—165°/0·1 mm., m. p. 48—48·5° (from aqueous ethanol) (Found: C, 80·1; H, 14·1. $C_{19}H_{40}O$ requires C, 80·3; H, 14·1%), was converted into the iodide which by condensation with ethyl methylmalonate afforded *ethyl 2-carbethoxy-2 : 4-dimethyleicosanoate*, b. p. 198—201°/0·15 mm. (Found: C, 74·3; H, 12·3. $C_{27}H_{52}O_4$ requires C, 73·6; H, 11·8%). This, by the usual successive stages, gave 2 : 4-dimethyleicosanoic acid, b. p. 195—198°/0·15 mm. (Found: C, 78·0; H, 12·9. $C_{22}H_{44}O_2$ requires C, 77·6; H, 12·9%). Its *amide*, after crystallisation from ethanol, had m. p. 79° (Found: C, 78·0; H, 13·4. $C_{23}H_{45}ON$ requires C, 77·9; H, 13·3%).

The preceding acid gave *via* the bromo-acid bromide by the procedure previously described *methyl 2-bromo-2 : 4-dimethyleicosanoate*, b. p. 194—199°/0·1 mm. (Found: C, 63·5; H, 10·3; Br, 18·7. $C_{23}H_{45}O_2Br$ requires C, 63·7; H, 10·4; Br, 18·3%). This, on pyridine dehydrobromination, followed by hydrolysis of the resulting unsaturated ester, afforded *2 : 4-dimethyleicos-2-enoic acid*, b. p. 199—201°/0·1 mm., m. p. 53—54° (Found: C, 78·1; H, 12·3. $C_{22}H_{42}O_2$ requires C, 78·1; H, 12·4%), $\log \varepsilon_{max.}$ 4·07 at 2140 Å. The *amide*, after crystallisation from ethanol, had m. p. 82° (Found: C, 78·4; H, 12·6; N, 4·1. $C_{22}H_{43}ON$ required C, 78·3; H, 12·8; N, 4·2%).

2 : 4-Dimethyldocos-2-enoic Acid (II; $n = 17$).—2 : 4-Dimethyldocosanoic acid (Bailey, Polgar, and Robinson, *loc. cit.*) on α-bromination, followed by pyridine dehydrobromination as described above for similar cases, afforded methyl 2 : 4-dimethyldocos-2-enoate, b. p. 172—176°/0·07 mm., which was hydrolysed to *2 : 4-dimethyldocos-2-enoic acid*, m. p. 63·5—64° (from light petroleum, b. p. 40—60°) (Found: C, 78·9; H, 12·6. $C_{24}H_{46}O_2$ requires C, 78·7; H, 12·6%), $\log \varepsilon_{max.}$ 4·13 at 2160 Å. The *amide* formed needles, m. p. 85—85·5° (from ethanol) (Found: C, 79·1; H, 12·5; N, 3·8. $C_{24}H_{47}ON$ requires C, 79·0; H, 12·9; N, 3·8%). The *dimethylamide*, which did not crystallise satisfactorily, distilled at 220° (bath)/0·04 mm. (Found: N, 3·6. $C_{26}H_{51}ON$ requires N, 3·6%).

2 : 4-Dimethyldocosanoic acid (see above) gave an *amide* which crystallised from ethanol in needles, m. p. 77·5—79° (Found: C, 78·3; H, 13·1; N, 3·5. $C_{24}H_{49}ON$ requires C, 78·5; H, 13·4; N, 3·8%). Its *dimethylamide* distilled at 220—224° (bath)/0·04 mm. (Found: C, 78·4; H, 13·1; N, 3·8. $C_{26}H_{53}ON$ requires C, 79·0; H, 13·4; N, 3·5%).

Amines.—A solution of the requisite amide (2 g.) in ether or tetrahydrofuran (100 c.c.) was added dropwise to a suspension of lithium aluminium hydride (0·6 g.) in boiling ether (50 c.c.), the resulting mixture refluxed for 105 min., then cooled, and the excess of lithium aluminium hydride decomposed by the addition of ethyl acetate. A few c.c. of water were then added, followed by " Hyflosupercel " (1 g.). The ethereal solution was decanted from the precipitate, and the latter washed with ether; the solution and washing were combined, dried (Na_2SO_4) and

evaporated. The resulting crude amine was dissolved in light petroleum (b. p. 40—60°), and 10% ethanolic hydrogen chloride added until precipitation was complete. Thus were obtained: *2-Methyleicosylamine hydrochloride*, fine needles (from acetone–alcohol), m. p. 107·5—108·5° (Found: C, 72·6; H, 13·3; N, 3·7; Cl, 10·3. $C_{21}H_{46}NCl$ requires C, 72·5; H, 13·2; N, 4·0; Cl, 10·2%), *2-methyleicosyldimethylamine hydrochloride*, needles (from acetone), m. p. 176—178° (Found: C, 73·6; H, 13·3; N, 3·4; Cl, 8·8. $C_{23}H_{50}NCl$ requires C, 73·5; H, 13·3; N, 3·7; Cl, 9·4%), *2-methyleicos-2-enylamine hydrochloride* (III), needles (from acetone), m. p. 109—110° (Found: C, 73·1; H, 13·0; N, 4·0; Cl, 10·1. $C_{21}H_{44}NCl$ requires C, 73·0; H, 12·7; N, 4·0; Cl, 10·3%), *2-methyleicos-2-enyldimethylamine hydrochloride* (IV), needles (from acetone), m. p. 168—169° (Found: C, 73·5; H, 12·6; N, 3·8; Cl, 9·9. $C_{23}H_{48}NCl$ requires C, 73·9; H, 12·9; N, 3·7; Cl, 9·5%), *2 : 4-dimethyldocosylamine hydrochloride*, needles (from acetone), m. p. 71—73° (Found: C, 73·7; H, 13·2; N, 3·4. $C_{24}H_{52}NCl$ requires C, 73·9; H, 13·4; N, 3·6%), *2 : 4-dimethyldocosyldimethylamine hydrochloride*, m. p. 151—153° (from acetone) (Found: C, 74·8; H, 13·6; N, 3·2; Cl, 8·3. $C_{26}H_{56}NCl$ requires C, 74·7; H, 13·4; N, 3·4; Cl, 8·5%), *2 : 4-dimethyldocos-2-enylamine hydrochloride* (V), m. p. 58—60° (from acetone) (Found: C, 74·3; H, 12·9; N, 3·4; Cl, 8·1. $C_{24}H_{50}NCl$ requires C, 74·3; H, 12·9; N, 3·6; Cl, 9·2%), and *2 : 4-dimethyldocos-2-enyldimethylamine hydrochloride* (VI), m. p. 147—150° (from acetone) (Found: C, 75·0; H, 12·8; N, 3·3; Cl, 9·0. $C_{26}H_{54}NCl$ requires C, 75·1; H, 13·0; N, 3·4; Cl, 8·6%).

The infrared spectrum of 2 : 4-dimethyldocos-2-enylamine showed a weak band at 1660 cm.$^{-1}$ (C=C) which was absent in case of the corresponding saturated base.

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The Oxidation of Hydrazine in Aqueous Solution. Part III. Some Aspects of the Kinetics of Oxidation of Hydrazine by Iron*(III) *in Acid Solution.*

By W. C. E. Higginson and P. Wright.

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Rates of formation of iron(II) and ammonia in the oxidation of hydrazine by iron(III) in acid solution have been measured. The results show that formation of ammonia proceeds through the dimerisation of N_2H_3 radicals. Under the conditions of these experiments, disproportionation of N_2H_3 radicals is unimportant. The latter finding is not in accord with the conclusions of other workers, and this disagreement is discussed.

The mechanism of oxidation of hydrazine in acid solution can be partly established by using isotopically distinguished nitrogen (Higginson and Sutton, *J.*, 1953, 1402; Cahn and Powell, *J. Amer. Chem. Soc.*, 1954, **76**, 2568). The latter authors obtained further information by kinetic studies. We now report similar studies which lead us to somewhat different conclusions.

The experiments using labelled nitrogen show that oxidation by a 1-electron-transfer reagent can be expressed in terms of two limiting overall reactions:

$$\text{(i)}\quad N_2H_4 \xrightarrow{-(e)} \tfrac{1}{2}N_2 + NH_3$$

$$\text{(ii)}\quad N_2H_4 \xrightarrow{-4(e)} N_2$$

In (i), $NH_2{\cdot}NH{\cdot}NH{\cdot}NH_2$ is an intermediate, and successively loses two ammonia molecules, forming nitrogen gas. The experiments do not show how this intermediate is formed, although 1-electron oxidation of hydrazine, followed by dimerisation of the resulting N_2H_3 radicals, appears to be the most likely mechanism. Both atoms in a nitrogen molecule formed in (ii) come from the same hydrazine molecule, but it is not possible to decide whether the probable intermediate, N_2H_2 (cf. Part I, *J.*, 1953, 1380), is

* Part II, *J.*, 1953, 1402.

formed by further oxidation of N_2H_3, or by disproportionation between two N_2H_3 radicals, or by both these routes.

These uncertain aspects of the oxidation mechanism can be investigated by kinetic experiments. Iron(III) appeared to be the only suitable 1-electron oxidant, although preliminary experiments showed that iron(II) retarded the reaction, presumably by reducing N_2H_3 to N_2H_4. The mechanism can thus be plausibly represented as :

$$Fe(III) + N_2H_4 \xrightarrow{k_1} Fe(II) + N_2H_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$Fe(II) + N_2H_3 \xrightarrow{k_{-1}} Fe(III) + N_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (-1)$$

$$2N_2H_3 \xrightarrow{k_2} N_4H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

followed by

$$N_4H_6 \xrightarrow{\text{fast}} N_2 + 2NH_3$$

$$2N_2H_3 \xrightarrow{k_3} N_2H_2 + N_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

followed by

$$N_2H_2 \xrightarrow{-2(e),\ \text{fast}} N_2$$

$$Fe(III) + N_2H_3 \xrightarrow{k_4} N_2H_2 + Fe(II) \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

followed by

$$N_2H_2 \xrightarrow{-2(e),\ \text{fast}} N_2$$

The reaction $N_2H_2 + N_2H_4 \longrightarrow N_4H_6$ is not included, since with 2-electron oxidants no ammonia is formed under conditions similar to those in our experiments, although N_2H_2 is thought to be the primary intermediate in such reactions (Part I, *loc. cit.*). Apart from the introduction of the back reaction (−1), this sequence is the same as that proposed by Cahn and Powell (*loc. cit.*). Unlike these workers, who measured overall stoicheiometries, we have investigated the dependence of the rates of formation of iron(II) and ammonia upon reactant concentrations. [For this purpose we include iron(II) as a reactant.] If the above mechanism is correct :

$$R(NH_3) = k_2[N_2H_3]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and

$$R(Fe) = k_1[Fe(III)][N_2H_4] - k_{-1}[Fe(II)][N_2H_3] + k_3[N_2H_3]^2 + 3k_4[Fe(III)][N_2H_3] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where $R(NH_3) = d[NH_3]/dt$, $R(Fe) = d[Fe(II)]/dt = -d[Fe(III)]/dt$

Making the stationary state assumption, we have

$$0 = d[N_2H_3]/dt = k_1[Fe(III)][N_2H_4] - k_{-1}[Fe(II)][N_2H_3] - k_2[N_2H_3]^2 - k_3[N_2H_3]^2 - k_4[Fe(III)][N_2H_3] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

k_1 and k_{-1} can be eliminated from (6), giving

$$R(Fe) = k_2[N_2H_3]^2 + 2k_3[N_2H_3]^2 + 4k_4[Fe(III)][N_2H_3] \quad . \quad . \quad . \quad (8)$$

Dividing (8) by (5), we have

$$R(Fe)/R(NH_3) = 1 + 2k_3/k_2 + 4k_4[Fe(III)]/k_2[N_2H_3] \quad . \quad . \quad . \quad (9)$$

and, eliminating $[N_2H_3]$ by use of (5) :

$$R(Fe)/R(NH_3) = 1 + 2k_3/k_2 + 4k_4[Fe(III)]/\sqrt{k_2R(NH_3)} \quad . \quad . \quad (10)$$

Fig. 1 shows a plot (full line) of $R(Fe)/R(NH_3)$ against $[Fe(III)]/\sqrt{R(NH_3)}$ for experiments in chloride-ion solutions, summarised in Table 1. We consider that the resulting linear

plot provides good evidence that the above reaction scheme is valid, for we are unable to suggest a different mechanism similarly consistent with our experimental results. The intercept, $(1 + 2k_3/k_2)$, is seen to be near to unity and was evaluated by rewriting equation (10) in the form :

$$\frac{R(\mathrm{Fe})}{[\mathrm{Fe(III)}]\sqrt{R(\mathrm{NH_3})}} = \left(1 + \frac{2k_3}{k_2}\right)\frac{\sqrt{R(\mathrm{NH_3})}}{[\mathrm{Fe(III)}]} + \frac{4k_4}{\sqrt{k_2}} \quad . \quad . \quad . \quad (11)$$

a plot of the left-hand side against $\sqrt{R(\mathrm{NH_3})}/[\mathrm{Fe(III)}]$ then giving as gradient $(1 + 2k_3/k_2) = 1{\cdot}03 \pm 0{\cdot}03$. Hence $k_3/k_2 = 0{\cdot}015 \pm 0{\cdot}015$.

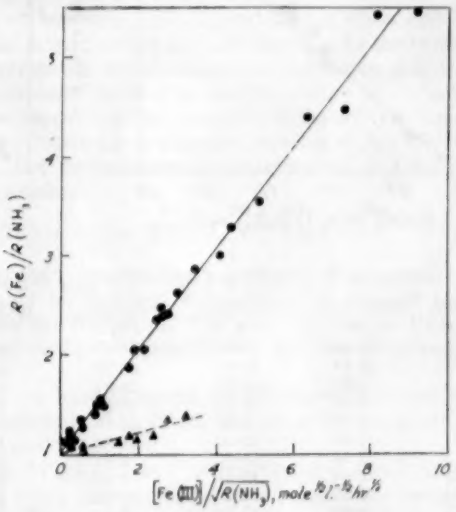

FIG. 1.
● *Chloride solution.*
▲ *Sulphate solutions.*

At sufficiently high concentrations of iron(II) the rate of disappearance of N_2H_3 by reactions (2), (3), and (4) will be very much less than by (−1), and as an approximation, if $K = k_1/k_{-1}$:

$$[\mathrm{N_2H_3}] = K[\mathrm{Fe(III)}][\mathrm{N_2H_4}]/[\mathrm{Fe(II)}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

From (12) and (5) :

$$R(\mathrm{NH_3}) = k_2K^2[\mathrm{Fe(III)}]^2[\mathrm{N_2H_4}]^2/[\mathrm{Fe(II)}]^2 \quad . \quad . \quad . \quad . \quad . \quad (13)$$

and from (12) and (9) :

$$R(\mathrm{Fe})/R(\mathrm{NH_3}) = 1 + 2k_3/k_2 + 4k_4[\mathrm{Fe(II)}]/Kk_2[\mathrm{N_2H_4}] \quad . \quad . \quad . \quad (14)$$

The expression $R(\mathrm{N_2H_4})/\{k_1[\mathrm{Fe(III)}][\mathrm{N_2H_4}] - R(\mathrm{N_2H_4})\}$, represented by $R(2,3,4)/R(-1)$, gives the ratio of the rate of disappearance of N_2H_3 radicals by reactions (2), (3), and (4) to the rate of disappearance by (−1), and its value can be used to indicate whether (12) is an allowable approximation. $R(\mathrm{N_2H_4})$ can be obtained from $R(\mathrm{NH_3})$ and $R(\mathrm{Fe})$, since $R(\mathrm{N_2H_4}) = \frac{3}{4}R(\mathrm{NH_3}) + \frac{1}{4}R(\mathrm{Fe})$. It is difficult to find k_1 directly at 60°; however, experiments at 25° and 35° with low iron(II) concentrations and under otherwise similar conditions gave $k_1 = 0{\cdot}06$ and $0{\cdot}35$ l. mole^{-1} hr.$^{-1}$, whence at 60° $k_1 \simeq 18$ l. mole^{-1} hr.$^{-1}$. The experiments in Table 1 are arranged in increasing order of the $R(2,3,4)/R(-1)$ values which vary from 5×10^{-3} to $5{\cdot}4 \times 10^{-2}$. These approximate figures suggest that (12) is a reasonable assumption for the first experiments in Table 1. Figs. 2 and 3 show that equations (13) and (14) hold well for experiments 1—6. Equation (14) holds fairly well for all the experiments in Table 1, and gives an intercept similar to that obtained by using equation (10), but deviations, increasing with $R(2,3,4)/R(-1)$, of up to 35% in $R(\mathrm{NH_3})$ occur from equation (13). These plots give additional evidence for the validity of the

proposed reaction mechanism. The effect of iron(II) when in concentrations comparable with those of the other reactants is also emphasised, whereas (10) should hold even in the absence of reaction (—1).

The value of 0·015 for k_3/k_2 obtained by using chloride-ion solutions at 60° compares poorly with Cahn and Powell's value of 0·15 found at 50° by using sulphate solutions.

FIG. 2.

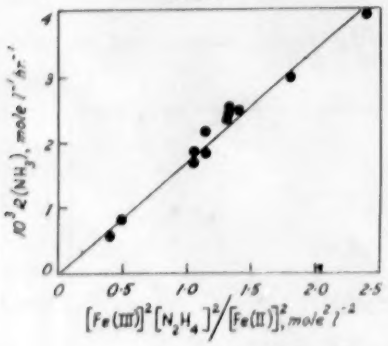

FIG. 3.

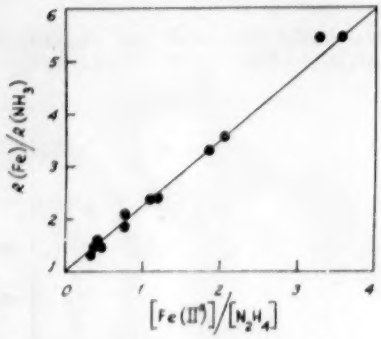

TABLE 1. $[H^+] = 1{\cdot}00$M; $[Cl^-]_{total} = 3{\cdot}50$M; Temp. = 60°.

Expt.	Time, hr.	10^3[Fe(III)], M	10^3[Fe(II)], M	10^3[N_2H_4], M	$10^3R(NH_3)$	10^3R(Fe) (all in mole l^{-1} $hr.^{-1}$)	$10^3R(N_2H_4)$
1	1½	12·94	29·51	26·29	2·51	5·98	3·38
	2½	12·40	30·05	25·97	2·15	5·15	2·90
2	1½	8·60	19·70	26·37	2·43	4·57	2·97
	2½	8·16	20·15	26·11	1·84	3·75	2·32
3	1	4·27	9·89	26·60	2·38	3·35	2·62
	2	3·96	10·20	26·36	1·82	2·73	2·05
4	1½	22·93	10·02	3·07	0·80	4·33	1·68
	2½	22·54	10·41	2·92	0·60	3·30	1·23
5	1½	6·33	10·60	25·92	3·95	5·99	4·46
	2½	5·83	11·10	25·55	3·00	4·50	3·38
6	1½	21·73	11·02	6·00	2·47	8·11	3·88
	2½	21·06	11·69	5·69	1·70	6·06	2·79
7	1½	2·31	5·22	26·46	1·90	2·50	2·05
	2½	2·09	5·43	26·29	1·42	1·83	1·52
8	1½	22·35	7·51	2·93	1·23	5·42	2·28
	2½	21·92	7·94	2·74	0·90	4·04	1·69
9	1½	17·15	8·09	5·93	2·45	7·00	3·59
	2½	16·56	8·68	5·63	1·66	5·00	2·50
10	1½	12·76	5·95	6·02	2·44	6·01	3·33
	2½	12·25	6·47	5·74	1·66	4·34	2·33
11	1½	12·19	4·59	5·65	3·28	6·73	4·14
	2½	11·63	5·15	5·31	2·12	5·00	2·84
12	1½	0·77	2·23	26·56	1·32	1·57	1·41
	2½	0·64	2·36	26·45	0·82	1·01	0·87
13	1	1·42	2·35	26·47	3·15	3·40	3·21
	2	1·15	2·61	26·22	1·75	2·00	1·81
14	1½	0·54	1·35	26·54	1·29	1·46	1·33
	2½	0·43	1·47	26·44	0·73	0·83	0·76

TABLE 2. $[H^+] + [HSO_4^-] = 1{\cdot}60$M; $[SO_4^{=}] + [HSO_4^-] = 1{\cdot}10$M; Temp. = 50°.

Expt.	Time, hr.	10^3[Fe(III)], M	10^3[Fe(II)], M	10^3[N_2H_4], M	$10^3R(NH_3)$	10^3R(Fe) (all in mole l^{-1} $hr.^{-1}$)	$10^3R(N_2H_4)$
15	1½	16·08	5·75	3·17	3·44	4·62	3·74
	2½	15·68	6·15	2·86	2·38	3·28	2·61
16	1	13·71	3·30	3·17	5·13	5·88	5·32
	2	13·23	3·77	2·75	3·13	3·70	3·27
17	1	9·18	2·91	3·42	3·81	4·25	3·92
	2	8·81	3·28	3·10	2·55	3·01	2·67
18	1½	2·76	2·06	7·13	2·84	3·02	2·89
	2½	2·50	2·32	6·87	2·20	2·28	2·22

Although it seemed to us that such a variation in conditions could not cause so big a change in the ratio of velocity constants involving only one reactant species, we completed four experiments, summarised in Table 2, under similar conditions to certain of Cahn and Powell's experiments. The corresponding plot of $R(\mathrm{Fe})/R(\mathrm{NH_3})$ against $[\mathrm{Fe(III)}]/\sqrt{R(\mathrm{NH_3})}$ is shown as the broken line in Fig. 1. In a similar manner to the interpretation of the chloride-ion experiments, we conclude that $k_3/k_2 = -0{\cdot}005 \pm 0{\cdot}025$. Since negative values are inadmissible, k_3/k_2 must lie between 0 and 0·02. Comparison of the rates of hydrazine disappearance at 1 (or $1\frac{1}{2}$) and 2 (or $2\frac{1}{2}$) hours in experiments 15—19 shows that there is a very much bigger change than can be accounted for by the change in the product of iron(III) and hydrazine concentrations, and hence that retardation by iron(II) is important at these concentrations in sulphate solutions.

We ascribe the difference between our value of k_3/k_2 and that of Cahn and Powell to their neglect of reaction (−1) in the interpretation of their results. As the concentration of iron(II) increases during their experiments, the stationary concentration of N_2H_3 radicals will fall relatively to the value to be expected in the absence of reaction (−1). Reference to equation (9) then shows that, as the overall reaction proceeds, $R(\mathrm{Fe})/R(\mathrm{NH_3})$ values in the presence of reaction (−1) will increase relatively to the corresponding $R(\mathrm{Fe})/R(\mathrm{NH_3})$ values in the absence of this reaction. The instantaneous stoicheiometry, $R(\mathrm{Fe})/R(\mathrm{N_2H_4})$, is related to $R(\mathrm{Fe})/R(\mathrm{NH_3})$ by the expression :

$$R(\mathrm{Fe})/R(\mathrm{N_2H_4}) = 4/\{1 + 3R(\mathrm{NH_3})/R(\mathrm{Fe})\} \quad . \quad . \quad . \quad . \quad (15)$$

and hence will increase more rapidly than their treatment suggests. The overall stoicheiometry is therefore higher than would be observed if reaction (−1) did not take place. Since Cahn and Powell do not allow for this effect, they can only ascribe their limiting overall stoicheiometry of 1·21 to a significant contribution by the disproportionation reaction (3).

At *ca.* 20° in sulphate solutions we have observed overall stoicheiometries as low as 1·03 when using cerium(IV) and cobalt(III). Simple calculation using (15) and (9) shows that under these conditions k_3/k_2 cannot exceed 0·02.

The experiments discussed above do not give any information about the charge on the various radicals and intermediates, which may act as acids or bases. We have therefore represented them as uncharged, and, for convenience, hydrazine as N_2H_4 although in our conditions $N_2H_5^+$ and $N_2H_6^{++}$ are present.

Experimental

Hydrazine dihydrochloride (from B.D.H.) was twice recrystallised. In stock solutions, hydrazine, chloride ion, and hydrogen ion in excess of that bound as $N_2H_5^+$ were determined by appropriate titrations. Iron(II) chloride and iron(II) sulphate stock solutions were prepared by dissolving weighed amounts of Hilger H.H.P. iron in excess of hydrochloric or sulphuric acid. Iron(III) chloride and iron(III) sulphate stock solutions were prepared by oxidation of the corresponding iron(II) solutions with inhibitor-free hydrogen peroxide, the excess of which was removed by gentle heating. Iron(II), iron(III), and hydrogen ion were determined in these stock solutions by appropriate methods. These iron solutions were kept in absence of light, the iron(II) solutions under nitrogen. All other stock solutions were made up from " AnalaR " reagents, and concentrations were determined where necessary by appropriate methods.

In the kinetic experiments in chloride-ion solutions a constant initial hydrogen-ion concentration was desired, and hence it was necessary to know the second dissociation constant of hydrazine, $K_2 = [\mathrm{H^+}][\mathrm{N_2H_5^+}]/[\mathrm{N_2H_6^{++}}]$, since the initial concentration of this reagent was varied from 0·269M to 0·0336M in different experiments. By using picric acid as an indicator, K_2 was estimated as 6 ± 2 mole $\mathrm{l.^{-1}}$ at 60° and ionic strength 3·5 by measurement of the optical density of solutions at 360 mμ. A Unicam SP500 spectrophotometer was used for these and other optical measurements. The initial hydrogen-ion concentration was 1·00; the error due to the uncertainty in K_2 is ±0·012M. Changes due to liberation of hydrogen ions during reaction were not greater than 0·03M-$\mathrm{H^+}$.

Iron(III) forms various complexes with chloride ions (Gamlin and Jordan, *J.*, 1953, 1435) and a high concentration of chloride ions was therefore used to minimise changes in the

proportion of these complexes and to maintain a high ionic strength. Sodium chloride was used to bring the total concentration of chloride ions to 3·50M. The maximum concentration of iron(III) used was 0·23M, and experiments showed that, with such an excess of chloride over iron(III), alterations of the order 10% in the chloride-ion concentration, with consequent changes in the ionic strength, caused negligible changes in the rate of reaction. The ionic strength of the solutions cannot be estimated accurately but is probably slightly less than 3·5 and does not vary greatly from one experiment to another.

In the reactions in sulphate solutions a large excess of sulphate could not be used. From Whiteker and Davidson's results (*J. Amer. Chem. Soc.*, 1953, **75**, 3081) we conclude that in these solutions iron(III) is mainly in the form $Fe(SO_4)_2^-$. Accordingly, solutions were made up 1·60M in hydrogen ion, and twice the corresponding concentration of iron(III) plus 1·10M in sulphate ion, giving a concentration of free sulphate plus bisulphate of 1·10M. The second dissociation constant of sulphuric acid increases considerably with ionic strength (Bray and Liebhafsky, *ibid.*, 1935, **57**, 51), and under our conditions is probably of the order 0·1—0·3 mole $l.^{-1}$. Hence the free hydrogen-ion concentration lies within the range 0·5—0·8M.

Reactions were carried out under pure nitrogen in absence of light. A mixture of all the reagents except the appropriate hydrazine stock solution was outgassed with nitrogen and allowed to come to equilibrium in a thermostat, and the reaction was started by adding the outgassed hydrazine solution. Two samples were withdrawn for ammonia and iron analyses within a few minutes of mixing. For most of the experiments four other pairs of samples were withdrawn at hourly intervals.

Ammonia was estimated in one of the samples in the following manner. Hydrazine was removed by addition of a small excess of potassium iodate and the iodine so formed by sodium sulphite. Excess of sulphite was removed by boiling. The solution was transferred to a small distillation apparatus and made alkaline with sodium hydroxide. Ammonia was distilled into 2% boric acid solution and titrated with 0·01M-hydrochloric acid with mixed bromocresol-green and methyl-red indicator following Ma and Zuazaga's method (*Ind. Eng. Chem. Anal.*, 1942, **14**, 280).

Iron(II) or iron(III), depending on which was present in smaller amount, was estimated in the second sample. Iron(II) was estimated by measurement of the optical density at 510 mμ of the tris-*o*-phenanthroline complex in a citrate buffer (Brandt and Smith, *Analyt. Chem.*, 1949, **21**, 1313). Iron(III) was estimated by measurement of the optical density at 303 mμ of a sample diluted in 0·4M-sulphuric acid. The extinction coefficient of such iron(III) sulphate solutions varies with temperature (Dewhurst, *Trans. Faraday Soc.*, 1953, **49**, 1175), and is affected slightly by the presence of low concentrations of chloride ions as obtained in diluted samples from the experiments in chloride-ion solutions. Appropriate calibration curves were made to correct for these two effects. Iron(II), iron(III), and ammonia were analysed by using the above methods in solutions of known composition, similar in all respects to those of the reaction solutions. We conclude that iron(II) and iron(III) can be determined in the reaction solutions with an accuracy of ±1%, and ammonia with an accuracy of ±2%.

Plots of the iron and ammonia concentrations against time were made from these results, and the gradients found at the times quoted in Tables 1 and 2. Since only a part of the reaction was followed, the changes in rates were not large in a given experiment. In most cases these changes were not greater than three-fold and were never larger than six-fold. We consider that $R(NH_3)$ can be estimated to ±5% and R(Fe) to ±6% from these plots. Since there is a comparatively small change in $R(Fe)/R(NH_3)$ over a given experiment, this quantity can be compared with $\Delta[Fe(II)]/\Delta[NH_3]$ values taken over hourly intervals, and we conclude that $R(Fe)/R(NH_3)$ can be obtained to ±5%.

THE UNIVERSITY, MANCHESTER, 13.

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Compounds of Tertiary Amines with Nitrosyl Chloride and with Dinitrogen Tetroxide.

By Alan E. Comyns.

[Reprint Order No. 5569.]

Aliphatic and aromatic tertiary amines react with nitrosyl chloride and with dinitrogen tetroxide in inert solvents at −78° to give coloured addition compounds. That from trimethylamine and dinitrogen tetroxide has the formula NMe_3,N_2O_4, and that from dimethylaniline and nitrosyl chloride has the formula $NPhMe_2,NOCl$. By measurement of electrical conductances and absorption spectra the nitrosyl chloride and dinitrogen tetroxide complexes of dimethylaniline were shown to be the nitrosammonium salts $[NPhMe_2{\cdot}NO]^+ X^-$ ($X^- = Cl^-$ or NO_3^-).

Although addition compounds of amines with oxides of nitrogen and related species have been postulated as intermediates in the reactions of amines with nitrosating agents (Donald and Reade, *J.*, 1935, **56**; Crowley, Milton, Reade, and Todd, *J.*, 1940, 1288; Lamberton and Wright, *Canad. J. Res.*, 1948, **26**, 110; Glazer, Hughes, Ingold, James, Jones, and Roberts, *J.*, 1950, 2671), little work has been directed towards their isolation. The addition compounds of tertiary amines would be expected to be more stable than those of other amines, and these alone have now been investigated.

Jones and Whalen (*J. Amer. Chem. Soc.*, 1925, **47**, 1345) obtained an orange solid by mixing ethereal solutions of trimethylamine and nitrosyl chloride at −78°, which, on warming, became brown and then decomposed yielding nitric oxide, formaldehyde, trimethylammonium chloride, dimethylammonium chloride, and chloromethyldimethylamine. These products are similar to those of the reaction between trimethylamine and hypochlorous acid (Meisenheimer, *Ber.*, 1913, **46**, 1148). Dimethylaniline, with nitrosyl chloride, yields dimethyl-*p*-nitrosoaniline (Neber and Rauscher, *Annalen*, 1942, **550**, 182); and with dinitrogen tetroxide yields a mixture of nitroso- and nitro-compounds (Schaarschmidt, Balzerkiewicz, and Gante, *Ber.*, 1925, **58**, 499). Battegay and Kern (*Bull. Soc. chim.*, 1928, **43**, 114) found that when the latter reaction was carried out in benzene solution below 10° the mixture was initially brown and then rapidly became green.

Since our work was completed, Sisler, Burkhardt, and Davenport (*J. Amer. Chem. Soc.*, 1953, **75**, 4175) have reported addition compounds of dinitrogen tetroxide with heterocyclic amines and with triethylamine; and Addison, Hodge, and Sheldon (*Chem. and Ind.*, 1953, 1338) have commented on the difference between the formulæ of the complexes obtained by these workers and those obtained in the present work, as described in a preliminary note (Comyns, *Nature*, 1953, **172**, 491).

Earlier work on reactions between pyridine and oxides of nitrogen includes Spencer's claim (*Chem. News*, 1903, **87**, 176) to have isolated a white addition product with dinitrogen tetroxide; Schaarschmidt *et al.* (*loc. cit.*) stated that the already known addition product with dinitrogen tetroxide did not rearrange to give 3-nitropyridine; Shorigen and Topschiew (*Ber.*, 1936, **69**, 1874), studied gas-phase reactions of pyridine with dinitrogen tetroxide and obtained 3-nitropyridine and pyridinium nitrate; and Haines and Adkins (*J. Amer. Chem. Soc.*, 1925, **47**, 1419) isolated an addition compound with dinitrogen pentoxide, which, however, might have been pyridinium nitrate (Haines, Thesis, Wisconsin, 1924, p. 15).

Experimental

Materials.—Dinitrogen tetroxide was prepared by dropping fuming nitric acid on damp sodium nitrite, and distilling the product over phosphoric oxide in a stream of oxygen until it gave a white solid on cooling. Nitrosyl chloride was prepared by the method of *Inorg. Synth.*, 1939, **1**, 53, and freed from hydrogen chloride by prolonged refluxing in a current of nitrogen. Trimethylamine was refluxed with acetic anhydride and then distilled through a tube packed with mercuric oxide and barium oxide. Triethylamine was distilled from barium oxide. Dimethylaniline, refluxed with acetic anhydride and fractionated, had b. p. 192—193°, n_D^{25} 1·5556. Dimethyl-*o*-toluidine (B.D.H.) was purified by von Braun and Aust's method (*Ber.*, 1914, **47**,

260); the two fractions collected in the final distillation had n_D^{25} 1·5230 (cf. n_D^{25} 1·5153 given by von Braun *et al.*, *loc. cit.*, and n_D^{20} 1·5255 by Ley and Pfeiffer, *Ber.*, 1921, **54**, 371). Dimethylmesidine was synthesised from mesitylene by nitration, reduction, and methylation, and the crude product was refluxed with acetic anhydride: fractionation yielded a product of b. p. 212—213°. Diethylaniline and *N*-methyldiphenylamine were dried over potassium hydroxide, and distilled under reduced pressure. The three dimethylnitroanilines and dimethyl-*p*-nitrosoaniline were kindly supplied by Dr. E. L. Blackall. Pentane was prepared from "standard pentane" by treatment with nitrating acid for two months, followed by alkaline permanganate; after drying (P_2O_5), the product was fractionated and the fraction of b. p. $< 40°$ was collected. *s*-Tetrachloroethane was dried ($CaCl_2$) and distilled under reduced pressure. Ethyl chloride and methylene chloride were dried (P_2O_5) and distilled. Acetonitrile was dried (K_2CO_3) and fractionated, it had b. p. 81·0—81·3°/744 mm., n_D^{25} 1·3422.

Introductory Experiments.—Solutions of the reactants in corked test-tubes were cooled in solid carbon dioxide and alcohol and then mixed. Some of the experiments on the trimethylamine–dinitrogen tetroxide system were performed in an all-glass system with rigid exclusion of moisture, and results identical with those of similar experiments in test-tubes were obtained.

Dinitrogen tetroxide solutions in ether and in pentane, when mixed at −78° with solutions of trimethylamine and triethylamine in excess, gave pale yellow precipitates and solutions. When the mixtures were warmed to *ca.* −55° the precipitates became brown, and further warming caused the colour completely to fade and nitric oxide to be evolved. Trimethylamine and triethylamine, treated with an excess of dinitrogen tetroxide in ether at −78°, gave yellow products similar to those produced when the amine was present in excess, but on warming to *ca.* −55° the precipitates became more dense and assumed a flesh colour. These new precipitates were relatively stable and began to decompose at *ca.* −5°, evolving oxides of nitrogen and leaving cream-coloured solids. Our attention to these reactions in the presence of excess of dinitrogen tetroxide was first drawn by the work of Sisler *et al.* (*loc. cit.*), and we therefore did not further examine the flesh-coloured precipitates.

Some of the white solid produced by the reaction of dinitrogen tetroxide with trimethylamine in excess was prepared in an all-glass system in order to exclude moisture. Trimethylamine (0·36 g. in 5 ml.) and dinitrogen tetroxide (0·28 g. in 5 ml.) were mixed in carbon tetrachloride at *ca.* −25°: a gelatinous brown solid resembling precipitated ferric hydroxide was produced. This solid was filtered off and washed with cold carbon tetrachloride while still at *ca.* −25° by means of a sintered-glass disc in the base of the reaction tube which was immersed in the cold bath. The filtrate and washings required 12·1 ml. of 0·107N-sulphuric acid for neutralisation. The remaining brown solid was allowed to warm slowly to room temperature: nitric oxide was evolved and a sticky, deliquescent, white solid (0·33 g.) remained. Recrystallisation *in situ* from dry acetonitrile yielded crystals of m. p. 130° which were not deliquescent; a second recrystallisation yielded crystals of m. p. 153°, mixed m. p. with trimethylammonium nitrate 153°. By analogy with the work of Jones and Whalen (*loc. cit.*) the deliquescent component of the crude white solid was probable dimethylammonium nitrate.

Dimethylaniline, diethylaniline, dimethyl-*p*-nitrosoaniline, and *N*-methyldiphenylamine reacted with nitrosyl chloride and with dinitrogen tetroxide solutions at −78° to give complexes of a very intense dark red colour, which were soluble in halogenated hydrocarbons (*e.g.*, ethyl chloride, methylene chloride, *s*-tetrachloroethane–ether), but sparingly soluble in hydrocarbons and in ether. These complexes were more stable than those of the aliphatic amines, and could be kept for several hours at −78° without visible change. When the complex of dimethylaniline with nitrosyl chloride was warmed above −78° its red colour was replaced by the green colour of dimethyl-*p*-nitrosoaniline. When solutions of nitrosyl chloride and dimethylaniline were mixed at room temperature a transient red colour was observed before the green colour appeared.

Dimethylmesidine gave yellow complexes with nitrosyl chloride and with dinitrogen tetroxide at −78°, resembling those of the aliphatic amines. Their colour faded on slight warming, nitric oxide was evolved, and white solid remained. The solid from the nitrosyl chloride complex was recrystallised from acetonitrile and yielded dimethylmesidinium chloride, m. p. 153—155°, picrate, m. p. 181—183°, [Emerson *et al.* (*J. Amer. Chem. Soc.*, 1941, **63**, 972) give m. p. 155—156°, picrate, m. p. 181—182°].

Dimethyl-*o*-toluidine gave a vermilion precipitate with a solution of nitrosyl chloride in ether at −78°. On slight warming, the colour faded to orange, and nitric oxide was evolved, but on cooling again to −78° the vermilion colour reappeared. This process was repeated several times until the vermilion colour failed to reappear on cooling. This amine was the only one of those examined to show this reversible colour change.

There was no visible reaction between solutions of the three dimethylnitroanilines and nitrosyl chloride or dinitrogen tetroxide at −78°.

Combining Ratios.—The molecular ratios in which the reactants had combined in two of the complexes were determined as follows. Known quantities of the two reactants were mixed at −78° or −100° in pentane, and that in excess was quantitatively removed by high-vacuum distillation through a short-path apparatus into a trap cooled in liquid air, the reaction vessel being kept at −78° or −100°. The excess, which had collected in the liquid-air trap, was then determined. The two systems studied by this method were that of dinitrogen tetroxide with trimethylamine in excess, and of dimethylaniline with nitrosyl chloride in excess.

Trimethylamine–dinitrogen tetroxide. The solution of trimethylamine was stored in, and delivered from, an automatic pipette fitted with a jacket containing ice and water. It was standardised by delivering aliquot parts into an excess of hydrochloric acid and back-titration with standard alkali (methyl-red). The dinitrogen tetroxide solutions were standardised by Milligan's method (*J. Phys. Chem.*, 1924, **28**, 554); 2-ml. aliquot parts were pipetted into concentrated sulphuric acid (5 ml.) contained in a small stoppered flask cooled in ice, and the mixture was gently agitated until the brown fumes had disappeared. The solution was then poured into potassium permanganate solution (100 ml. of *ca.* 0·05N) with rapid stirring, the flask was washed twice with sulphuric acid, and the washings were added to the solution. An excess of ferrous sulphate solution was then added and the excess determined by titration with permanganate. In the distillation experiments 5-ml. aliquot parts of the amine solution were delivered into the reaction vessel (a 1″ test-tube with a B29 socket) cooled to −100°: this temperature was attained by cooling a solid carbon dioxide–ethanol bath by liquid air contained in a small metal pot. The dinitrogen tetroxide solution (2 ml.) was added slowly with gentle shaking; it was allowed to run down the cold walls of the reaction vessel before meeting the amine solution. With continuous evacuation by a mercury-vapour diffusion pump about 30 min. sufficed for all of the solvent and the trimethylamine in excess to have distilled into the receiver (a 2″ test-tube made from a B55 socket). The complex was left adhering to the walls of the reaction tube as a dry, brown powder which rapidly became white after removal of the cold bath. The distillate was pale yellow, showing that some volatilisation of dinitrogen tetroxide had occurred. The amine in the distillate was determined by absorption into hydrochloric acid and back-titration with alkali: the error due to the presence of the small amount of dinitrogen tetroxide was probably negligible. The results are given in Table 1. There is considerable scatter in the values for the combining ratio, but

TABLE 1. *Trimethylamine with dinitrogen tetroxide.*

N_2O_4 taken	NMe_3 taken	NMe_3 recovered	Initial ratio	Final ratio	N_2O_4 taken	NMe_3 taken	NMe_3 recovered	Initial ratio	Final ratio
0·00	10·6	10·5	—	—	1·88	3·63	1·49	1·9	1·14
5·81	8·75	3·60	1·5	0·89	1·92	4·02	2·24	2·1	0·92
3·59	5·47	2·11	1·5	0·94	1·46	5·13	3·59	2·9	1·05
5·61	8·50	3·00	1·5	0·98					

Quantities are expressed in moles × 10^{-3}. "Ratio" refers to mole ratio $NMe_3 : N_2O_4$.

these are fairly evenly distributed about unity, and we conclude that the compound NMe_3,N_2O_4 is formed at −100°. It would have been desirable to have repeated the experiments but with dinitrogen tetroxide in excess: this was not attempted as the simple apparatus employed was unsuitable for the quantitative absorption of dinitrogen tetroxide.

Dimethylaniline–nitrosyl chloride. The nitrosyl chloride solutions were stored in and delivered from the cooled automatic pipette. They were standardised by absorption into sodium hydroxide solution at 0°, and Volhard titration of the chloride ion thereby produced. Dimethylaniline was delivered from a weight pipette into the reaction tube, solvent was added, and the solution was cooled to −78°. The distillation procedure was similar to that described above. At the conclusion of a distillation the receiver was removed, silver nitrate solution was added, and a bung was quickly inserted into the neck. On warming to room temperature, the nitrosyl chloride reacted with the melting silver nitrate solution, and the remaining silver nitrate was then determined by thiocyanate titration. The results are given in Table 2. They show that with pentane as solvent a 1 : 1 complex is formed, but that with ethyl chloride and methylene chloride less than one equivalent of nitrosyl chloride remains with the dimethylaniline. Continued pumping of the solid after all of the solvent had been removed did not result in the removal of any more nitrosyl chloride. If, however, solvent was continually added as it distilled out and the mixture was never allowed to become dry, nitrosyl chloride could continuously be removed: this was the method by which the value of 0·52 was obtained for the

combining ratio in ethyl chloride, and 0·91 in pentane. Pure solid nitrosyl chloride can rapidly be removed under these conditions and so could not have been present as such in the remaining red solids. The red solids rapidly became green after removal of the cold bath.

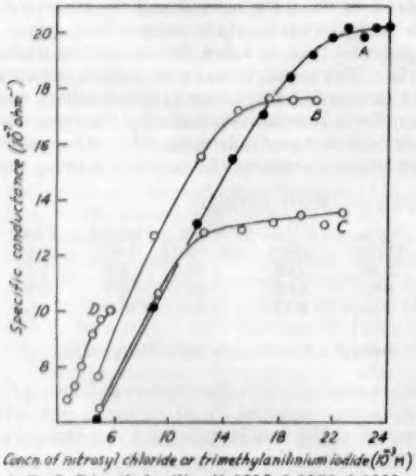
TABLE 2. *Dimethylaniline with nitrosyl chloride.*

$NPhMe_2$ taken	NOCl taken	NOCl recovered	Initial ratio	Final ratio	Solvent	Volume of solvent (ml.)
0·00	2·28	2·26	—	—	C_5H_{12}	5
1·21	2·12	0·84	1·75	1·06	,,	10
1·59	2·42	0·68	1·53	1·09	,,	10
1·21	2·31	1·03	1·88	1·06	,,	10
1·18	2·27	1·09	1·92	1·00	,,	17
1·19	2·14	1·06	1·80	0·91	,,	20
1·41	2·48	1·25	1·75	0·87	C_2H_5Cl	10
1·03	2·43	1·65	2·36	0·76	,,	10
1·20	2·42	1·80	2·02	0·52	,,	20
1·83	2·92	1·23	1·60	0·92	CH_2Cl_2	10
1·85	2·88	1·17	1·55	0·92	,,	10

Quantities are expressed in moles $\times 10^{-3}$. " Ratio " refers to mole ratio NOCl : $NPhMe_2$.

Measurements of Electrical Conductance.—Conductance measurements were made on the system dimethylaniline–nitrosyl chloride and related systems at −78°, and the results are shown in Figs. 1 and 2. The solvent was prepared by diluting *s*-tetrachloroethane (170 ml.) with ether to 250 ml. As much heat is liberated on mixing, the final few ml. of ether were not added until

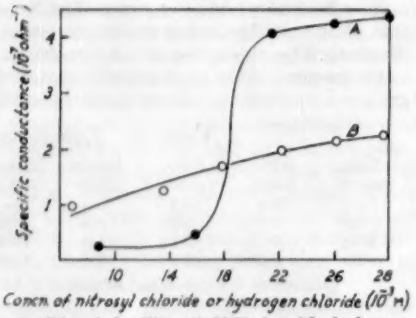
FIG. 1.



Concn. of nitrosyl chloride or trimethylanilinium iodide (10^{-3}M)

A, B, C, Dimethylaniline (0·0216, 0·0158, 0·0110M respectively) with nitrosyl chloride.
D, Trimethylanilinium iodide.

FIG. 2.



Concn. of nitrosyl chloride or hydrogen chloride (10^{-3}M)

A, Dimethylaniline (0·0179M) with hydrogen chloride.
B, Nitrosyl chloride.

the bulk of the mixture had re-attained room temperature. A correction was applied for the contraction of the solvent on cooling from 0° or 20°, at which the solutions were prepared or standardised, to −78°: Dr. I. G. Ross of this Department found that 1 ml. at 20° occupied 0·903 ml. at −78°, and that 1 ml. at 0° occupied 0·922 ml. at −78°. All measurements were made by using as a thermostat a Dewar vessel containing a stirred slurry of solid carbon dioxide and ethanol, the temperature of which was found to vary from −78° to −80°. The cell was similar to the Shedlovsky pattern, constructed from a 100-ml. flask attached by a capillary tube to the electrode compartment of 5 ml. capacity. The electrodes were parallel plates of bright platinum. The cell-constant was measured at 0°, with N/100-potassium chloride solution as the standard, and found to be 0·186 $cm.^{-1}$. This value was used without correction for calculating specific conductances at −78°. Measurements of resistance lower than 3×10^5 ohm were made on an

A.C. bridge at 1000 c.p.s. Measurements of resistance higher than this were made on a D.C. bridge incorporating a 6-valve amplifier, constructed by Mr. B. Eisler of this Department.

(a) *Trimethylanilinium iodide.* A solution was prepared containing 0·35 g. of the crystalline salt, m. p. 235° (decomp.), in 25 ml. of solution, and 15 ml. of this were delivered into the cell. Conductance measurements were made on this solution and after successive dilutions by solvent.

(b) *Nitrosyl chloride.* The cell initially contained solvent (12 ml.), and aliquot parts of nitrosyl chloride solution (1 ml. of 0·0823M at 0°) were successively added. The conductance observed may have been due to the ionisation $NOCl \rightleftharpoons NO^+ Cl^-$, but as great care was not taken in purifying the solvent the measurements are of little quantitative significance. The specific conductance at 0·02M was $1·8 \times 10^{-7}$ ohm^{-1}, which may be compared with the value of 6×10^{-7} ohm^{-1} found by Seel (*Z. anorg. Chem.*, 1944, **252**, 39) for a solution of nitrosyl chloride of this concentration in sulphur dioxide at −70°.

(c) *Dimethylaniline–nitrosyl chloride.* In each of three experiments the amine concentration was kept constant while that of the nitrosyl chloride increased and measurements were made at different nitrosyl chloride concentrations. These conditions were obtained by the following procedure. Two amine solutions were prepared, one of exactly twice the concentration of the other, and the more dilute solution was contained in the conductance cell. The nitrosyl chloride solution was added to this in 1-ml. aliquot parts, as also was the more concentrated amine solution. In one experiment dimethylaniline solution (7·5 ml., containing 0·0615 g. to 25 ml.) and solvent (7·5 ml.) were delivered into the cell and successive additions made of both nitrosyl chloride solution (0·0823M at 0°) and amine solution. The conductance of the dimethylaniline solutions rose sharply with increase in nitrosyl chloride concentration until equivalent quantities were present, and then remained nearly constant. It would probably have continued to rise slowly were it not for the simultaneous slow decomposition of the complex, which process causes a fall in conductance.

(d) *Dimethylaniline–hydrogen chloride.* The procedure was similar to that used with nitrosyl chloride. The conductance of the dimethylanilinium chloride formed under these conditions was much smaller than that of the dimethylaniline–nitrosyl chloride complex. The greater conducting power of quaternary ammonium salts over those containing a bound proton is familiar (cf., *e.g.*, Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 21).

Absorption Spectra.—Qualitative observations were made of the absorption spectra of dimethylaniline solutions with added nitrosyl chloride and dinitrogen tetroxide. The solvent was the same *s*-tetrachloroethane–ether as was used for the conductance measurements. The solutions were prepared and kept at −78°, and measurements were made with a Cary recording spectrophotometer.—I am indebted to Dr. R. Passerini for them. The cell was designed by Dr. I. G. Ross. It had a continuously evacuated outer jacket of stainless steel, enclosing the two brass cells surrounded by coolant. Amine was present in excess in both experiments, and the spectrophotometer recorded the difference in the absorption between the amine solution and a similar solution containing added nitrosyl chloride or dinitrogen tetroxide. Similar spectra were obtained whether nitrosyl chloride or dinitrogen tetroxide was employed: the solution containing nitrosyl chloride exhibited a sharp maximum at 398 mμ and that containing dinitrogen tetroxide gave a similar maximum at 404 mμ. These results indicate that the same species is responsible for the colour of both solutions. Addison *et al.* (*loc. cit.*) have pointed out that the complex of dinitrogen tetroxide with diethylnitrosamine also has an absorption maximum in this region (at 412 mμ).

Discussion

The analytical results show that dimethylaniline and nitrosyl chloride form a 1 : 1 addition compound at −78°, and the similarity of the electrical conductance of this adduct to that of a uni-univalent quaternary ammonium salt indicates that it is the nitrosammonium salt $[NPhMe_2 \cdot NO]^+Cl^-$. The similarity between the absorption spectra of the nitrosyl chloride and the dinitrogen tetroxide adduct of dimethylaniline indicates that the latter adduct has the analogous formula $[NPhMe_2 \cdot NO]^+NO_3^-$.

The fact that the combining ratio of nitrosyl chloride to dimethylaniline, as measured in the analytical experiments, was less than unity when halogenated solvents, in which the complex is soluble, were employed in place of pentane, in which the complex is sparingly soluble, indicates that an equilibrium may exist in solution:

$$RR'R''N + NOX \rightleftharpoons RR'R''N \cdot NO^+ X^-$$

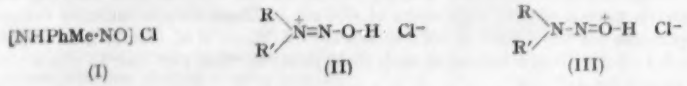
An alternative explanation is that solid complexes containing less than one molecule of nitrosyl chloride to one of dimethylaniline are formed under these conditions.

The decomposition products of the complexes of the aromatic amines were not examined in detail, but are probably identical with the products obtained when the reactants are mixed at room temperature. The complexes of the aliphatic amines and of dimethylmesidine, which in many ways resembles an aliphatic amine, are much less stable than those of the aromatic amines; and their decomposition products correspond closely with those predicted by Ingold *et al.* (*loc. cit.*) for the nitrosammonium ions which were postulated as intermediates in the oxidative de-alkylation of aromatic amines during nitrosation and nitration.

The reversible phenomena encountered in the dimethyl-*o*-toluidine–nitrosyl chloride system may be explained by the low reactivity of this amine toward nitrosating agents. Dimethyl-*o*-toluidine, as is well known (cf., *e.g.*, von Braun, Arkuszewski, and Kohler, *Ber.*, 1918, **51**, 282), is resistant to nuclear nitrosation. It is usually supposed, therefore, that it is inactive toward nitrous acid (Hickinbottom, " Reactions of Organic Compounds," Longmans, London, 1948, p. 318), but it has been found (unpublished results) that products analogous to those produced by the action of nitrous acid on dimethyl-*p*-toluidine (Crowley *et al.*, *loc. cit.*) are formed, although at a much slower rate than nuclear nitroso-compounds are formed by related amines.

The substances prepared by Sisler *et al.* (*loc. cit.*) from dinitrogen tetroxide and triethylamine have properties different from those of the compounds obtained in the present work. Our observation that pink substances are formed from trimethylamine and triethylamine in the presence of an excess of dinitrogen tetroxide, at about the temperature at which the initial yellow complexes decompose, suggests that the substances analysed by Sisler *et al.* might not have been simple addition compounds but were more complex substances produced by reactions between dinitrogen tetroxide and the decomposition products of the addition compounds. Addison and Hodge (*Chem. and Ind.*, 1953, 1315) have obtained the yellow compound $N_2O_4,2(Et_3NH{\cdot}NO_3),4Et_2O$ which, they point out, is closely related to one of the substances obtained by Sisler *et al.* The analytical procedure used by Sisler *et al.* could not be used for the complexes which we, and Jones and Whalen, obtained, since in this procedure the reaction mixture warms to a temperature considerably above −75° during the filtration, and extensive decomposition with loss of nitric oxide would occur.

The hydrochloride of methylphenylnitrosamine has been formulated as the nitrosammonium salt (I) (Neber and Rauscher, *loc. cit.*), but as this and other nitrosamine hydrochlorides are relatively stable substances and unlike the complexes obtained in the present work it seems unlikely that they have similar formulæ. It is therefore suggested that in the nitrosamine hydrochlorides the protons are attached to the oxygen atoms, and that resonance between structures (II) and (III) occurs:



A substance (II) is isoelectronic with a ketone oxime, and similarities would therefore be expected between the infrared spectra of nitrosamine hydrochlorides and ketone oximes with similar alkyl groups.

The author thanks Professor C. K. Ingold, F.R.S., and Professor E. D. Hughes, F.R.S., for their suggestion of the problem and for much helpful advice and criticism.

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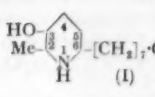
Stereochemistry of Carpamic Acid.

By T. R. Govindachari and N. S. Narasimhan.

[Reprint Order No. 5897.]

Carpamic acid is shown to have the substituents at $C_{(2)}$ and $C_{(6)}$ *cis* to each other. On the basis of negative evidence the 3-hydroxyl group is assigned the equatorial conformation.

Carpamic acid (I), obtained by hydrolysis of the alkaloid carpaine, has three asymmetric centres. It was desired in the first instance to convert carpamic acid into deoxycarpamic acid under conditions which would preserve the configuration at $C_{(2)}$ and $C_{(6)}$. Although ethyl carpamate was recovered unchanged after treatment with thionyl chloride, ethyl *N*-methylcarpamate was converted by this reagent into ethyl chlorodeoxy-*N*-methylcarpamate which could be reduced catalytically to ethyl deoxy-*N*-methylcarpamate. Crystalline derivatives of the last compound suitable for characterisation could not be prepared, the salts being highly hygroscopic. However, treatment with cyanogen bromide effected smooth demethylation yielding ethyl (−)-deoxycarpamate, characterised as hydrochloride.



(I)

Deoxycarpyrinic acid [ω-(6-methyl-2-pyridyl)octanoic acid], obtained by dehydrogenation of carpaine (Rapaport and Baldridge, *J. Amer. Chem. Soc.*, 1952, **74**, 5365), was reduced catalytically in an acid medium to racemic deoxycarpamic acid, the product being isolated as the ethyl ester hydrochloride. A single product was obtained in quantitative yield. Since catalytic reduction of 2 : 6-disubstituted pyridines in acid medium leads only to the *cis*-isomers (Scheuing and Winterhalder, *Annalen*, 1929, **473**, 126), the substituents in racemic ethyl deoxycarpamate obtained by this method should have a *cis*-relation to each other. This was confirmed by reducing deoxycarpyrinic acid with sodium and alcohol: fractional crystallisation of the product, isolated as the ester hydrochloride, yielded a hydrochloride, m. p. 127—128°, identical with the catalytic reduction product, and a second hydrochloride, m. p. 83—85°. Since the melting-point behaviour of *cis-trans* pairs is reversed in the case of 1 : 3-disubstituted *cyclo*hexanes and 2 : 6-disubstituted piperidines, the higher-melting hydrochloride should be that of the 2 : 6-*cis*-isomer.

The infrared spectrum of racemic ethyl *cis*-deoxycarpamate hydrochloride was identical with that of the (−)-isomer prepared as indicated above. This is clear proof that in carpamic acid, the 2- and the 6-substituent have a *cis*-relationship and both may be said to be equatorial.

The resistance to dehydration exhibited by carpamic acid (Barger, Robinson, and Work, *J.*, 1937, 711), the ready replacement of the hydroxyl group in ethyl *N*-methylcarpamate by chlorine, and the failure of ethyl carpamate to undergo epimerisation on prolonged heating with sodium pentyloxide all suggest that the hydroxyl group in carpamic acid is equatorial. Attempts to oxidise carpamic acid or its derivatives to the corresponding $C_{(3)}$ ketone have so far proved unfruitful and positive evidence for assigning the equatorial position to the hydroxyl group could not therefore be obtained.

Experimental

N-Methylcarpaine.—A mixture of carpaine (2 g.), formaldehyde (2·3 ml.), formic acid (2·3 ml.), and toluene (2 ml.) was refluxed (oil-bath) for 4 hr., after which it was cooled and poured into water (50 ml.). The mixture was rendered alkaline with sodium carbonate and extracted with benzene. The benzene extracted was washed once with water and, after drying (Na_2SO_4) and removal of the solvent, gave an oil which solidified. One crystallisation from acetone–water yielded *N*-methylcarpaine (2·05 g.), m. p. 84° (Found: C, 70·9; H, 10·4. Calc. for $C_{15}H_{27}O_2N$: C, 71·2; H, 10·7%) (m. p. 71° is given in "The Alkaloids, Chemistry and Physiology," Manske and Holmes, Academic Press, Inc., New York, 1950, Vol. I, p. 99).

N-Methylcarpamic Acid.—A solution of *N*-methylcarpaine (3·8 g.) in concentrated

hydrochloric acid (60 ml.) was refluxed for 3 hr., after which it was evaporated to dryness *in vacuo*. *N*-Methylcarpamic acid hydrochloride (3·8 g.) was thus obtained crystalline but extremely hygroscopic, and was converted directly into the ethyl ester.

Ethyl N-*Methylcarpamate.*—A solution of *N*-methylcarpamic acid hydrochloride (3·8 g.) in absolute alcohol (75 ml.) was saturated with dry hydrogen chloride at 0°. After 48 hr., the alcohol was distilled off. The residue was dissolved in water and, after basification with sodium carbonate, the base was extracted with benzene. On evaporation, drying (Na_2SO_4), and distillation, *ethyl* N-*methylcarpamate* (3·8 g.), b. p. 146—150°/0·3 mm., was obtained (Found: C, 68·0; H, 11·0. $C_{17}H_{33}O_3N$ requires C, 68·2; H, 11·0%).

Ethyl Chlorodeoxy-N-methylcarpamate.—Ethyl *N*-methylcarpamate (3·8 g.) in chloroform (5 ml.) was cooled in ice and treated with thionyl chloride (1·2 ml.) drop by drop with shaking. Next morning the mixture was poured into ice-water (25 ml.) and extracted with ether. The acid extract was rendered alkaline with sodium carbonate and extracted with ether. Drying (Na_2SO_4) and evaporation of the ether extract gave a dark brown oil (3 g.) which on fractionation yielded ethyl *N*-methylcarpamate (500 mg.), b. p. 148°/0·3 mm., and then the crude chloro-compound (2 g.), b. p. 170—200°/0·3 mm. Refractionation yielded *ethyl chlorodeoxy-N-methylcarpamate* (1·6 g.), b. p. 190—200°/0·3 mm. (Found: C, 64·0; H, 11·3. $C_{17}H_{32}O_2NCl$ requires C, 64·3; H, 10·1%).

Ethyl Deoxy-N-methylcarpamate.—Crude chloro-compound (2 g.) in absolute alcohol (30 ml.) was shaken with Adams catalyst (0·3 g.) in hydrogen at 60 lb. for 6 hr. The solution was filtered and evaporated on a water-bath. The residue was suspended in a little water, rendered alkaline with sodium carbonate, and extracted with benzene. On evaporation of the benzene extract after drying (Na_2SO_4), a colourless oil (1·6 g.) was obtained. This on fractionation yielded fractions (i) (1·3 g.), b. p. 120—140°/0·3 mm., and (ii) (200 mg.), b. p. 148°/0·3 mm. The former yielded *ethyl deoxy-N-methylcarpamate* (800 mg.), b. p. 130°/0·3 mm., $[\eta]^{28}$ 1·448 (Found: C, 71·7; H, 11·8. $C_{17}H_{33}O_2N$ requires C, 72·1; H, 11·7%). The second fraction was ethyl *N*-methylcarpamate.

Ethyl (−)-*Deoxycarpamate.*—To a solution of cyanogen bromide (400 mg.) in absolute benzene (3 ml.) was added ethyl deoxy-*N*-methylcarpamate (800 mg.) in benzene (3 ml.) drop by drop with stirring. The mixture was kept overnight. On removal of the solvent an amber-coloured, non-basic liquid (800 mg.) was obtained, which did not contain bromine. This (800 mg.) was hydrolysed by boiling 20% sulphuric acid (10 ml.). The solution was cooled and, after dilution with water and extraction of the non-basic material with ether, was treated with a slight excess of barium chloride solution. The precipitated barium sulphate was filtered off, and the filtrate evaporated to dryness *in vacuo* The residue was esterified by the Fischer procedure, giving an oil (300 mg.) which was converted into the hydrochloride by the usual procedure. One crystallisation yielded pure *ethyl* (−)-*deoxycarpamate hydrochloride*, m. p. 130—131°, $[\alpha]_D^{28}$ −10·3° (*c*, 2·6 in EtOH) (Found: C, 62·6; H, 10·7. $C_{16}H_{32}O_2NCl$ requires C, 62·9; H, 10·5%).

Ethyl cis-(±)-*Deoxycarpamate.*—A solution of deoxycarpyrinic acid hydrochloride (1 g.) in absolute alcohol (35 ml.) containing 5 drops of concentrated hydrochloric acid was hydrogenated over Adams catalyst (200 mg.) at 60 lb. On filtration and evaporation racemic *ethyl* cis-*deoxycarpamate hydrochloride*, m. p. 123—126°, was obtained in quantitative yield. One crystallisation from alcohol–ether gave the pure compound, m. p. 127—128° (Found: C, 62·7; H, 10·1. $C_{16}H_{32}O_2NCl$ requires C, 62·9; H, 10·5%).

Reduction of Deoxycarpyrinic Acid with Sodium and Alcohol.—A solution of deoxycarpyrinic acid (1 g.) in alcohol was reduced by sodium (10 g.) in the usual way. The product isolated as the hydrochloride (800 mg.) was esterified by the Fischer procedure. Fractional crystallisation of the ester hydrochloride from alcohol–ether gave ethyl *cis*-deoxycarpamate hydrochloride (400 mg.), m. p. 128°, as the first fraction. This did not depress the m. p. of the compound obtained as above. From the mother-liquor *ethyl* trans-*deoxycarpamate hydrochloride* (300 mg.), m. p. 80—85°, was obtained. Two crystallisations from alcohol–ether raised the m. p. to 83—85° (Found: C, 63·1; H, 10·4%).

Action of Sodium Pentyloxide on Ethyl Carpamate.—A solution of sodium (2·5 g.) in pentanol (60 ml.) containing ethyl carpamate (700 mg.) was refluxed for 4 hr. Fractional crystallisation of the product gave a single compound, isolated as the hydrochloride, which was identical with the starting material (m. p. and mixed m. p.).

We thank Mr. Selvavinayagam for microanalysis. We are grateful to Professor Roger Adams and Dr. James J. Brader, University of Illinois, for the infrared absorption spectra,

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Polymerisation of Thiophen Derivatives. Part IV. The Formation of Some 9-Thia-1 : 2- and 9-Thia-3 : 4-benzofluorene Derivatives.*

By W. DAVIES, F. C. JAMES, S. MIDDLETON, and Q. N. PORTER.

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Though the usual products obtained by heating thionaphthen 1 : 1-dioxide (I) are sulphur dioxide and 10 : 11-dihydro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (II) (Part I), different conditions cause the formation of some 1 : 2-benzo-9-thiafluorene 9 : 9-dioxide (III). 3-Chloro- and 3- and 5-bromothionaphthen dioxides give good yields of 9-thia-3 : 4-benzofluorene derivatives, of which the structures have been proved. The self-condensation of thionaphthen dioxide derivatives is of wide application, though tars are sometimes the only organic products. New syntheses have been developed for related polycyclic sulphones and sulphoxides.

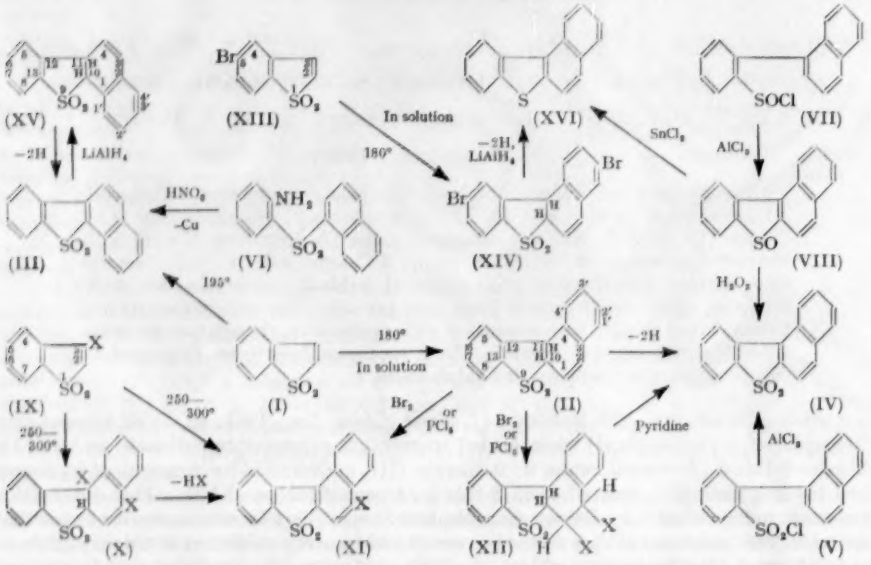
BORDWELL, MCKELLIN, AND BABCOCK (*J. Amer. Chem. Soc.*, 1951, **73**, 5566) showed that thionaphthen 1 : 1-dioxide (I) when heated in solution gives sulphur dioxide and 10 : 11-dihydro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (II), convertible by removal of hydrogen into the sulphone (IV) derived from 9-thia-3 : 4-benzofluorene (XVI). This observation was made independently by Davies, Gamble, and Savige (Part I), who moreover found that the tetracyclic sulphone (IV) is formed in small yield during oxidation of thionaphthen to its sulphone. An intermediate adduct of a Diels–Alder type is postulated, and Davies and James (Part II) have isolated such an intermediate in the simpler case of the oxidative conversion of thiophen into thionaphthen dioxide.

The tetracyclic compounds formed in good yield from simple thionaphthen dioxides have so far proved to be 3 : 4- and not 1 : 2-benzo-9-thiafluorene derivatives. Thus, 5-bromothionaphthen 1 : 1-dioxide (XIII) in solution about 180° gives 10 : 11-dihydro-2′ : 6-dibromo-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (XIV), whose 1 : 2-dibromide through dehydrobromination gives 2′ : 6-dibromo-9-thia-3 : 4-benzofluorene 9 : 9-dioxide. From this compound lithium aluminium hydride removes both oxygen and both bromine atoms, forming 9-thia-3 : 4-benzofluorene (XVI), a useful reference compound in this series (Part I).

The attempts of Bordwell *et al.* (*loc. cit.*) to extend the self-condensation reaction to thionaphthen dioxides other than (II) were unsuccessful, but in fact 3-halogenothionaphthen dioxides do react at an unusually high temperature. When 3-chlorothionaphthen 1 : 1-dioxide (IX; X = Cl) is heated alone at 280° it gives a 75% yield of 2 : 11-dichloro-10 : 11-dihydro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (X; X = Cl). Dehydrochlorination with pyridine converts this into 2-chloro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (XI; X = Cl), which is also produced by the interaction of (II) and phosphorus pentachloride, which here acts as a chlorinating and dehydrogenating agent (cf. Bert and Annequin, *Compt. rend.*, **1931**, **192**, 1107). The " dimerisation " of 3-bromothionaphthen 1 : 1-dioxide also requires a high temperature, and the tetracyclic dihydro-derivative has not been isolated in this case. Instead, the monobromo-compound (XI; X = Br) is obtained which, together with the tetrahydro-derivative (XII; X = Br), is obtained from the dihydro-compound (II) by use of bromine. The reaction chart oversimplifies the course of this halogenation, for which the experimental section should be consulted.

* The papers by Davies, Gamble, and Savige, *J.*, 1952, 4678, and by Davies and James, *J.*, 1954, 15, and *J.*, 1955, 314, are to be regarded as Parts I, II, and III, respectively.

The usual course of the formation of a 3 : 4-benzo-derivative of thiafluorene can be avoided when thionaphthen dioxide (I) is heated at 195° under special conditions. Instead of the tetracyclic dihydro-compound (II), there is formed a small yield of a compound now shown to be 9-thia-1 : 2-benzofluorene 9 : 9-dioxide (III). This structure has been proved by desulphurisation with Raney nickel to 2-phenylnaphthalene, and also by synthesis from



o-aminophenyl 1-naphthyl sulphone (VI) by a Pschorr type of reaction. Whereas the sulphone (IV) is readily reduced to the sulphide (XVI) by lithium aluminium hydride, the isomer (III) is merely reduced to 10 : 11-dihydro-9-thia-1 : 2-benzofluorene 9 : 9-dioxide (XV). Bromine converts this into the 3 : 4-dibromide which with boiling pyridine gives the original compound (III). Direct dehydrogenation by the use of *N*-bromosuccinimide can be of great value in this series, and instances will be given in a later communication.

It is to be expected that the sulphone group in the 1 : 2-benzo-derivative (III) would, through steric influences, be less easily attacked by certain reagents than that in the isomer (IV). This is true of alkali, but the completely different behaviour of the two compounds towards lithium aluminium hydride may serve as a reliable guide in predicting the 1 : 2- or the 3 : 4-position of the benzo-group in various thiafluorene 9 : 9-dioxide derivatives. Whereas the compounds (IV), (XI; X = Br), and (XIV; after preliminary removal of two hydrogen atoms) are converted into the reference compound (XVI), the sulphone group in the 1 : 2-benzothiafluorene derivative (III) remains intact. This last reaction is up to the present unique in this polycyclic series in that a dihydro-compound is formed; also a crimson colour develops during the reduction and persists until the reagent is destroyed on addition of water. The stereochemical course of reduction of several steroidal ketones by lithium aluminium hydride is thought to be due to the formation of an intermediate organometallic compound (*Ann. Reports*, 1953, **50**, 167), and perhaps the resistance to reduction shown by the sulphone group in the compound (III) is due to hindrance, by the neighbouring 1 : 2-benzo-group, of formation of such an intermediate. It may also be of general significance that Raney nickel removes the sulphone group from the compound (III), giving 2-phenylnaphthalene, because this reagent can be outstanding in overcoming steric effects, as for example in the reduction of the blocked ethylene oxide group in scopolamine (Fodor and Kovacs, *J.*, 1953, 2341). Reagents known to be either responsive or unresponsive to steric effects in certain fields may sometimes make unnecessary the rigid proof of

structure which has been provided for all the new compounds reported in this communication.

Among features of general interest in this work is the use of the Pschorr reaction for the cyclisation of aminoaryl sulphones, in which the yields so far have been between 20 and 30%. Dibenzothiophen 1 : 1-dioxide (9-thiafluorene 9 : 9-dioxide) was independently prepared by this method by the present authors and by de Tar and Sagmanli (*J. Amer. Chem. Soc.*, 1950, **72**, 965). It had also been prepared in small yield by an unintentional Pschorr synthesis by Ullmann and Pasdermadjian (*Ber.*, 1901, **34**, 1150). In the present work the tetracyclic compound (III) and an apparently new form of the isomer (IV) [the structure of which was shown by its conversion into the sulphide (XVI)] have been synthesised by the Pschorr cyclisation of the appropriate *o*-aminophenyl naphthyl sulphones. However, though the yield of five-membered rings produced by Pschorr cyclisations at present is often small (see also Hey and Mulley, *J.*, 1952, 2276; de Tar and Sagmanli, *loc. cit.*), this probably homolytic process of making cyclic sulphones is invaluable for determining chemical structure, and the yields should be capable of improvement.

Another useful synthesis is an internal Friedel–Crafts reaction to form cyclic sulphones. Chaix (*Bull. Soc. chim. France*, 1933, **53**, 700) obtained dibenzothiophen 1 : 1-dioxide from diphenyl-2-sulphonyl chloride. This rarely used reaction, which seems to be general and has been used to convert the chloride (V) into the sulphone (IV), is now of potential value as an alternative synthesis of polynuclear thiophen derivatives, which can often be formed by reduction of the corresponding sulphones with lithium aluminium hydride. A related and apparently novel process is the ring-closure, under Friedel–Crafts and related conditions, of diphenyl-2-sulphinyl chloride to form dibenzothiophen 1-oxide, and of *o*-1-naphthylbenzene-sulphinyl chloride (VII) to give 9-thia-3 : 4-benzofluorene 9-oxide (VIII). This process has an advantage over that requiring sulphonyl chlorides since the sulphoxides produced are, unlike sulphones, reducible to the sulphides by common reducing agents. Thus the sulphoxide (VIII) is rapidly reduced by stannous chloride, giving an excellent yield of the sulphide (XVI). However, both these Friedel–Crafts cyclisations involve the serious difficulty of previously preparing the acid chlorides with the sulphur-containing groups in the appropriate *ortho*-positions.

There is uncertainty in the literature about the properties or structure of the monochloro- and dichloro-derivatives of thionaphthen. From equimolar quantities of chlorine and thionaphthen Schlesinger and Mowry (*J. Amer. Chem. Soc.*, 1951, **73**, 2614) obtained a liquid monochlorothionaphthen whose dioxide had m. p. 158·5—160°. Hartough and Meisel (" Compounds with Condensed Thiophene Rings," Interscience Publ., New York, 1954, p. 164) refer to the m. p. 167—168·5° for the dioxide of 3-chlorothionaphthen recorded in a Ph.D. dissertation by Lampert. In the present work, 3-chlorothionaphthen 1 : 1-dioxide (IX; X = Cl), m. p. 166—167°, is formed in good yield from phosphorus pentachloride and 3-hydroxythionaphthen 1 : 1-dioxide (IX; X = OH), which was obtained on hydrolysis of 3-diethylaminothionaphthen 1 : 1-dioxide (Bordwell and Albisetti, *J. Amer. Chem. Soc.*, 1948, **70**, 1558), of known structure. Chlorination of thionaphthen with less than a mole of chlorine also gives a monochloro-derivative, the dioxide of which has m. p. 166—167°.

Dichlorination of thionaphthen gives a crystalline dichlorothionaphthen assumed (Komppa, *J. pr. Chem.*, 1929, **122**, 319; Schlesinger and Mowry, *loc. cit.*; Davies, Gamble, and Savige, *loc. cit.*, p. 4681) to be 2 : 3-dichlorothionaphthen (the last authors, through a clerical error, named it 3 : 5-dichlorothionaphthen). There is still no definite proof that the second chlorine atom entered at position 2. However, the dioxide (m. p. 160—161°) of the dichlorothionaphthen is, like that of 2-bromothionaphthen, remarkably stable to heat, and in small quantities can be distilled unchanged at ordinary pressure. All the thionaphthen dioxides of known structure so far investigated which contain a substituent in the benzene ring but have position 2 free are found to be readily decomposed by heat. This tends to support the otherwise very probable 2 : 3-dichloro-structure assigned previously.

The compound represented as 3-hydroxythionaphthen 1 : 1-dioxide (IX; X = OH) has been arbitrarily given the enol form. The dimethyl acetal (m. p. 142·5—143°) of the

corresponding ketone is obtained from 3-bromothionaphthen 1 : 1-dioxide (IX; X = Br) and methanolic potassium hydroxide. This acetal has the expected properties and it has been previously made (m. p. 144°) by Arndt and Martius (*Annalen*, 1932, **499**, 283) by base-catalysed addition of methanol to the non-aromatic double bond in the enol ether (IX; X = OMe). Hartough and Meisel (*op. cit.*, pp. 157—158) cast doubt on the existence of this acetal: however, its formation by either method presents no theoretical difficulties, though the process is unusual. A close analogy is the conversion, by methanolic alkali, of aliphatic 2-chlorovinyl ketones into 2-keto-acetals [$R{\cdot}CO{\cdot}CH{:}CHCl \longrightarrow R{\cdot}CO{\cdot}CH_2{\cdot}CH(OMe)_2$] (Nelles, B.P. 466,890/1937; Price and Pappalardo, *J. Amer. Chem. Soc.*, 1950, **72**, 2613).

Generally, thionaphthen dioxides, when heated, evolve sulphur dioxide which, with tars, are the only product so far identified from the dioxides of 3-methyl-, 3-methoxy-, 3-dimethylamino-, 3-piperidino-, and 6-nitro-thionaphthen. 2-Bromo- and 2 : 3-dichlorothionaphthen dioxide were extremely stable to heat. However, an account will shortly be submitted of pure polymerised products from derivatives of thionaphthen substituted in the benzene nucleus. From the point of view of possible carcinogen formation, not only are polycyclic sulphides themselves of interest, but removal of the sulphur atom followed by cyclisation opens up a new route to the synthesis of polycyclic hydrocarbons (Davies, Gamble, James, and Savige, *Chem. and Ind.*, 1952, 804). The type of polymerisation process, detailed in the present communication, is capable of wide extension both to simple thiophen derivatives and to tricyclic (and probably polycyclic) systems in which the benzo-group in benzothiophen is replaced by homocyclic or heterocyclic residues. This and related work is being continued.

Experimental

Preparation of Sulphones of Substituted Thionaphthens.—3-Bromothionaphthen 1 : 1-dioxide, m. p. 183·5—184° (Bordwell and Albisetti, *loc. cit.*), was converted into 3-dimethylamino- and 3-piperidino-thionaphthen 1 : 1-dioxides by their method. These two bases when heated gave tars and sulphur dioxide.

3-Bromothionaphthen 1 : 1-dioxide (0·7 g.) was converted into 3-methoxythionaphthen 1 : 1-dioxide in good yield (m. p. 219—220°) by refluxing it in methanol (10 ml.) containing potassium hydroxide (0·2 g.) for 1 hr. (cf. Bordwell and Albisetti, *ibid.*, p. 1558, who record m. p. 220°). For this reaction commercial methanol had been purified by mixing it with a little hydrochloric acid, distilling it, and redistilling it over potassium hydroxide.

The 2 ; 3-dihydro-3 : 3-dimethoxythionaphthen 1 : 1-dioxide (0·43 g.; m. p. 142·5—143°, from methanol), was obtained when the above process was repeated with commercial methanol (Found: C, 52·7; H, 5·1; S, 14·3. Calc. for $C_{10}H_{12}O_4S$: C, 52·6; H, 5·3; S, 14·05%). After 1 hour's heating on the water-bath with 2% hydrochloric acid it gave 3-hydroxythionaphthen 1 : 1-dioxide, m. p. and mixed m. p. 133—133·5° (from benzene).

3-Hydroxythionaphthen 1 : 1-dioxide, which is best made by hydrolysis of 3-diethylaminothionaphthen 1 : 1-dioxide (Bordwell and Albisetti, *loc. cit.*), sintered when strongly heated. If the compound existed in the keto-form, the usual type of self-condensation would not occur.

3-Chlorothionaphthen 1 : 1-dioxide, prisms, m. p. 166—167° (from benzene–light petroleum), was obtained (1·9 g., 83%) by refluxing 3-hydroxythionaphthen 1 : 1-dioxide (2·0 g.) with phosphorus pentachloride (4·0 g.) and phosphorus oxychloride (10 ml.) for 4 hr., and decomposing the cold product with ice. It was also prepared (m. p. and mixed m. p. the same) (Found: Cl, 17·7. Calc. for $C_8H_5O_2SCl$: Cl, 17·7%) by interaction of hydrogen peroxide in glacial acetic acid on the water-bath with 3-chlorothionaphthen made as follows:

Chlorine (2·5 l.; 0·75 mol.) in carbon tetrachloride (200 ml.) was added drop-wise to a stirred solution of thionaphthen (20 g., 1 mol.) in carbon tetrachloride (100 ml.). Stirring was continued for 8 hr., and the solution then kept overnight and fractionated. After removal of unchanged thionaphthen the fraction (b. p. 140—160°/13 mm.; 4 g.) was essentially 3-chlorothionaphthen, and the fraction of b. p. 200—220°/13 mm. solidified to needles, m. p. 53—54°, of practically pure 2 : 3-dichlorothionaphthen.

2 : 3-Dichlorothionaphthen 1 : 1-dioxide, made by the action of hydrogen peroxide in the usual way, had m. p. 157—158° (Found: Cl, 30·0. Calc. for $C_8H_4O_2SCl_2$: Cl, 30·2%). It distilled unchanged at 1 atm.

2-Bromothionaphthen 1 : 1-dioxide (Bordwell, Lampert, and McKellin, *J. Amer. Chem. Soc.*, 1949, **71**, 1702) can be distilled unchanged at 1 atm. in small quantities.

6-Nitrothionaphthen 1 : 1-dioxide, made by Challenger and Clapham's method (*J.*, 1948, 1615), readily forms tar and sulphur dioxide when heated.

6-*Amino* 2 : 3-*dihydrothionaphthen* 1 : 1-*dioxide*, pale yellow needles, m. p. 198—198·5° (from benzene), was formed when the above nitro-compound was reduced with tin and hot hydrochloric acid (Found : C, 52·7; H, 5·0. $C_8H_9O_2NS$ requires C, 52·4; H, 4·9%).

6-*Aminothionaphthen* 1 : 1-*dioxide* (Found : C, 53·3; H, 4·0. $C_8H_7O_2NS$ requires C, 53·0; H, 3·9%), yellow needles, m. p. 172·5—173° (from benzene), was formed when the above nitro-compound (3·0 g.) was shaken for 3 hr. with stannous chloride dihydrate (14·0 g.) in concentrated hydrochloric acid (25 ml.), and the solution then kept at room temperature for a further 8 hr. and made alkaline with sodium hydroxide (30%). It yielded 6-*acetamidothionaphthen* 1 : 1-*dioxide*, needles, m. p. 192—192·5° (from benzene), when refluxed with acetic anhydride containing pyridine (Found : N, 6·4. $C_{10}H_9O_3NS$ requires N, 6·3%). This and the parent amine decompose readily on being heated, and no crystalline derivative has been isolated.

Action of Heat on Thionaphthen Dioxide (I).—(*a*) 10 : 11-Dihydro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (II) is obtained in optimum yield (89%) by refluxing thionaphthen dioxide for 6 hr. in four times its wt. of *o*-dichlorobenzene (b. p. 176—180°).

(*b*) The dioxide (2·0 g.) in a Pyrex tube was placed in an oil-bath preheated to 195° ± 5°, and this temperature maintained until the evolution of sulphur dioxide was complete (about 20 min.). A dark yellow-green chloroform extract, partially decolorised with carbon, yielded a dark orange oil whose benzene solution, chromatographed on alumina, developed bands which fluoresced in ultraviolet light. The single yellow band was eluted by benzene, and the crude yellow solid (0·2 g.; m. p. 120—130°), after several crystallisations from methanol and further chromatography on alumina, gave 9-thia-1 : 2-benzofluorene 9 : 9-dioxide (III), colourless needles, m. p. 195·5—196° (from benzene), with a strong blue fluorescence in ultraviolet light [the yellow fluorescence recorded for this substance, m. p. 197° (Davies, Gamble, and Savige, *loc. cit.*), is due to traces of impurity] (Found : C, 72·3; H, 3·8. Calc. for $C_{15}H_{10}O_2S$: C, 72·2; H, 3·8%).

A phenolic oil, soluble in alkali and giving a purple colour with ferric chloride but no crystalline benzoyl derivative, was obtained by fusing the dioxide (III) with excess of potassium hydroxide at 400—420° for 5 min. Desulphurisation occurred when the dioxide (III) (0·1 g.) and activated Raney nickel (3 g.; Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013) in ethanol (100 ml.) were refluxed for 8 hr.; the organic residue of 2-phenylnaphthalene (from ethanol) had m. p. and mixed m. p. 102—103° (cf. Elks, Haworth, and Hey, *J.*, 1940, 1284).

Lithium aluminium hydride (0·5 g.) reduced the dioxide (III) (0·3 g.) in boiling ether (200 ml.) in 6 hr. to 10 : 11-*dihydro*-9-*thia*-1 : 2-*benzofluorene* 9 : 9-*dioxide* (XV) (0·15 g.), needles, m. p. 157—158° (from ethanol) (Found : C, 71·7; H, 4·5; S, 11·7. $C_{15}H_{12}O_2S$ requires C, 71·7; H, 4·5; S, 11·9%). Unlike the isomeric 3 : 4-benzo-compound (II), it was very resistant to boiling 10% sodium hydroxide solution, 75% being recovered after 5 hr. However, the filtrate on acidification yielded a small amount of an unstable oil, apparently a crude sulphinic acid, for it rapidly lost sulphur dioxide at room temperature, and when freshly isolated gave a red-brown precipitate with ethanolic ferric chloride.

Bromine (0·15 g.) and the dioxide (XV) (0·25 g.) in boiling carbon tetrachloride (10 ml.) (10 hr.) gave 3 : 4-*dibromo*-10 : 11-*dihydro*-9-*thia*-1 : 2-*benzofluorene* 9 : 9-*dioxide*, prisms (from benzene), m. p. 226—226·5° (Found : Br, 37·2. $C_{15}H_{12}O_2SBr_2$ requires Br, 37·4%). When this (0·1 g.) was refluxed with pyridine (2·5 ml.) for 8 hr., it re-formed the unsaturated compound (III), m. p. and mixed m. p. 195—196°.

Action of Phosphorus Pentachloride on 10 : 11-*Dihydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*Dioxide* (II).—Finely powdered phosphorus pentachloride (6·0 g.) and this dioxide (II) (3·0 g.) were heated at 160° for 10 min.; the glass formed on cooling was powdered and stirred with water (50 ml.), and the residual yellow compound dried over phosphoric oxide and extracted with absolute alcohol (4 × 50 ml.). The insoluble portion, twice crystallised from 2-methoxyethanol, gave plates (0·1 g.) of 2-*chloro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide* (XI; X = Cl), m. p. 294—295°, slightly soluble in benzene (Found : C, 64·0; H, 2·95. $C_{15}H_9O_2SCl$ requires C, 63·9; H, 3·0%).

The combined alcoholic filtrates, on cooling, deposited pale yellow needles, m. p. 226—228° (0·5 g.), whose solution in benzene was passed through a short column of alumina. The first 5 c.c. of eluate deposited colourless needles of 9-thia-3 : 4-benzofluorene 9 : 9-dioxide (IV), m. p. and mixed m. p. 234° (though described as pale yellow by Davies *et al.*, *loc. cit.*, p. 4678) (Found : C, 72·1; H, 4·0. Calc. for $C_{15}H_{10}O_2S$: C, 72·2; H, 3·8%).

The alcoholic filtrates, after concentration to 25 ml., gave the main product of the reaction, pale yellow crystals (1·9 g.), m. p. 171—172·5°, which from alcohol (charcoal) yielded colourless prisms of **1 : 2-*dichloro*-1 : 2 : 10 : 11-*tetrahydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide*** (XII; X = Cl), m. p. 173·5—174°, showing a strong blue fluorescence in diffused daylight (Found: C, 56·6; H, 3·9; S, 9·2. $C_{16}H_{12}O_2SCl_2$ requires C, 56·6; H, 3·55; S, 9·5%). It was dehydrochlorinated when refluxed with pyridine for 8 hr. or heated alone at 250° for 8 min. The alcoholic solution of the residue was clarified by charcoal. The product in both cases was the sulphone (IV), m. p. and mixed m. p. 234°.

Self-condensation of **3-*Chlorothianaphthen* 1 : 1-*Dioxide*** (IX; X = Cl).—The sulphone (1·0 g.) was heated in a Pyrex tube in 1-bromonaphthalene vapour (280°) for 10 min., the cooled melt was extracted with boiling benzene (500 ml.), and the concentrated extract (charcoal) on cooling gave prisms (0·63 g.; 75%) of **2 : 11-*dichloro*-10 : 11-*dihydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide*** (X; X = Cl), m. p. 270—271° (Found: C, 57·4; H, 2·9. $C_{16}H_{10}O_2SCl_2$ requires C, 57·0; H, 3·0%). It (120 mg.) was dehydrochlorinated by refluxing pyridine (10 ml.) (20 hr.), and the pyridine removed under reduced pressure. The benzene extract, clarified with carbon, gave prisms (80 mg.), m. p. 294—295°, of 2-chloro-9-thia-3 : 4-benzofluorene 9 : 9-dioxide (Found: Cl, 11·4. $C_{16}H_9O_2SCl$ requires Cl, 11·1%). It was identical (mixed m. p.) with the above product from the interaction of phosphorus pentachloride with the sulphone (II).

In a preliminary experiment pure 3-chlorothionaphthen dioxide, heated in an oil-bath at 260—280° for 30 min., gave, in addition to the above substance, m. p. 270—271°, a small amount of less soluble colourless crystals of unknown constitution, decomp. >300° (Found: C, 49·1; H, 2·8%).

Action of Bromine on **10 : 11-*Dihydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*Dioxide*** (II).—Bromine (0·5 ml.) and the dioxide (1·0 g.) were refluxed in carbon tetrachloride (20 ml.) for 6 hr. and the yellow crystals formed after cooling, together with those which separated when the mother-liquor was concentrated to 5 ml., were extracted with ethanol (100 ml.). The small insoluble portion was **2-*bromo*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide*** (XI; X = Br), which recrystallised from 2-methoxyethanol in needles, m. p. 309—310° (Found: C, 56·0; H, 2·65; S, 9·6. $C_{16}H_9O_2SBr$ requires C, 55·65; H, 2·6; S, 9·3%). The alcoholic extract, when concentrated to 25 ml., gave **1 : 2-*dibromo*-1 : 2 : 10 : 11-*tetrahydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide*** (XII; X = Br), m. p. 185·5—186° (0·85 g.) (Found: C, 45·1; H, 3·0; S, 7·2. $C_{16}H_{12}O_2SBr_2$ requires C, 44·9; H, 2·8; S, 7·5%). On further concentration of the alcoholic filtrate to 5 ml. an additional 0·1 g. thereof was obtained, together with about 5 mg. of colourless needles, m. p. 198—199°, which were separated by hand. This compound could not be obtained when the bromination was repeated. The present work showed that only in this respect was the bromination difficult to repeat, and this is in contrast to the experience of Bordwell, McKellin, and Babcock (*loc. cit.*), whose only product from the reaction was $C_{16}H_{12}O_2SBr_2$, m. p. 175—176°, which may be an impure specimen of our product (XII; X = Br).

The above dibromo-compound, m. p. 186° (0·25 g.), was refluxed with pyridine for 6 hr., and the product obtained after dilution with water gave needles (0·14 g., 90%) (from alcohol), m. p. 234° alone or mixed with the sulphone (IV). This is also formed by heating dibromide (XII; X = Br) alone at 190° for 10 min. It is noteworthy that the aromatic sulphone (IV) is recovered unchanged after 6 hours' refluxing with bromine (2 mols.) in carbon tetrachloride.

Self-condensation of **3-*Bromothionaphthen* 1 : 1-*Dioxide*** (IX; X = Br).—This sulphone (0·5 g.) was heated in a Pyrex tube at 290—300° for ½ hr., and the black residue extracted with ethanol (500 ml.). The extract was boiled with charcoal and after concentration and cooling yielded pale yellow needles (0·2 g.), m. p. 309—310° undepressed by admixture with the monobromo-derivative (XI; X = Br) (Found: C, 55·8; H, 2·8%).

5-Bromothionaphthen* 1 : 1-*Dioxide (XIII).—5-Bromothionaphthen (100 mg.), prepared by the cyclisation of 4-bromophenylthioacetaldehyde diethyl acetal (cf. Rabindran, Sunthankar, and Tilak, *Proc. Indian Acad. Sci.*, 1952, **36**, *A*, 405), was heated in glacial acetic acid (1·0 ml.) and hydrogen peroxide (0·25 ml.; 30%) for 1 hr. on the water-bath, giving an excellent yield of ***5-bromothionaphthen* 1 : 1-*dioxide***, in colourless needles, m. p. 144—144·5° (from aqueous alcohol) (Found: O, 13·2. $C_8H_5O_2SBr$ requires O, 13·1%). This (50 mg.) was heated under reflux in *o*-dichlorobenzene (1 ml.) until the evolution of sulphur dioxide ceased (3 hr.). The solution was diluted with an excess of light petroleum (b. p. 40—60°), and the precipitate of **2′ : 6-*dibromo*-10 : 11-*dihydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide*** (XIV), formed in good yield, recrystallised from alcohol in prisms, m. p. 228—229° (Found: C, 45·1; H, 2·5. $C_{16}H_{10}O_2SBr_2$ requires C, 45·1; H, 2·35%).

The structure was proved by dehydrogenation and then reduction. The product (XIV) (0·7 g.) was refluxed for 8 hr. with bromine (0·5 ml.) in carbon tetrachloride (50 ml.), and on cooling **1 : 2 : 2′ : 6-*tetrabromo*-1 : 2 : 10 : 11-*tetrahydro*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide** separated in good yield and then recrystallised from benzene in prisms, m. p. 239·5—240° (Found : Br, 54·7. $C_{16}H_{10}O_2SBr_4$ requires Br, 54·6%). It was refluxed for 6 hr. with 25 times its wt. of pyridine, and the product, precipitated by water, crystallised from benzene in needles of **2′ : 6-*dibromo*-9-*thia*-3 : 4-*benzofluorene* 9 : 9-*dioxide***, m. p. 354—355° (Found : C, 45·7; H, 2·3. $C_{16}H_8O_2SBr_2$ requires C, 45·3; H, 1·9%). This dibromo-sulphone (30 mg.) was refluxed for 8 hr. with lithium aluminium hydride (75 mg.) in tetrahydrofuran (10 ml.), and excess of hydride decomposed with moist ether; after acidification with dilute hydrochloric acid the non-aqueous layer yielded **9-thia-3 : 4-benzofluorene**, m. p. and mixed m. p. 102°.

Preparation of Cyclic Sulphones by the Pschorr Reaction.—(i) ***Preparation of the intermediate nitro-sulphones.*** *α-Naphthyl o-nitrophenyl sulphide*, deep-yellow prisms (from alcohol), m. p. 152—153°, separated (6·8 g., 84%) after 4 hours' refluxing of *o*-chloronitrobenzene (5 g.) and naphthalene-1-thiol (4·7 g.) in a mixture of 40% aqueous sodium hydroxide (10 ml.) and ethanol (10 ml.) (Found : N, 5·05. $C_{16}H_{11}O_2NS$ requires N, 5·0%). This sulphide (6·0 g.) was heated in glacial acetic acid (70 ml.) and hydrogen peroxide (8·0 ml. of 30%) for 1 hr. on the water-bath, and dilution with water gave *α-naphthyl o-nitrophenyl sulphone* (6·1 g.), needles (from alcohol), m. p. 128—129° (Found : C, 61·7; H, 3·5; S, 10·0%). The isomeric *β-naphthyl sulphone* (5·8 g.), needles (from alcohol), m. p. 143·5—144°, was similarly obtained from the corresponding sulphide already described (Davies, Gamble, and Savige, *loc. cit.*) (Found : C, 61·3; H, 3·5; O, 20·3. $C_{16}H_{11}O_4NS$ requires C, 61·4; H, 3·5; O, 20·4; S, 10·2%).

o-Nitrophenyl phenyl sulphide, m. p. 79—80°, was made by Roberts and Turner's process (*J.*, 1926, 1208) in the same yield (their m. p. was 79°), though 24% of the *o*-chloronitrobenzene was recovered unchanged by distillation under reduced pressure. The sulphide was converted by hydrogen peroxide, as above, into the *o*-nitro-sulphone, m. p. 146—147° (cf. Ullmann and Pasdermadjian, *Ber.*, 1901, **34**, 1154).

(ii) ***Preparation of the amino-sulphones.*** To a solution of α-naphthyl *o*-nitrophenyl sulphone (5·0 g.) in ethanol (120 ml.), zinc dust (4·0 g.) and concentrated hydrochloric acid (20 ml.) were added, and the suspension was refluxed until dissolution was effected, for which further additions of hydrochloric acid were required. The solution was evaporated to dryness on the water-bath and the last traces of free hydrochloric acid were removed by the addition of water and further evaporation. Crystallisation from alcohol gave *o-aminophenyl α-naphthyl sulphone*, prisms (3·8 g.), m. p. 177—178° (Found : C, 68·0; H, 4·5. $C_{16}H_{13}O_2NS$ requires C, 67·9; H, 4·6; N, 4·9%). The isomeric *β-naphthyl sulphone*, prisms (3·8 g.), m. p. 136—136·5°, was similarly obtained from β-naphthyl *o*-nitrophenyl sulphone (5·0 g.) (Found : C, 67·8; H, 4·6; N, 5·0%). *o*-Nitrophenyl phenyl sulphone (10 g.) was similarly reduced to the amino-sulphone (8·8 g.), m. p. 120—121° (Ullmann and Pasdermadjian, *loc. cit.*, give m. p. 122°).

(iii) *Cyclisation.* (*a*) *o*-Aminophenyl α-naphthyl sulphone (1·0 g.) in acetic acid (20 ml.) and concentrated hydrochloric acid (20 ml.) was diazotised at 0° with sodium nitrite (1·0 g.) in water (10 ml.), and the solution set aside at room temperature for 15 min. Copper powder (0·5 g.) was added, and the solution shaken for 15 min. The yellow solid formed gave an orange product (m. p. 150—158°, from alcohol), whose benzene solution was chromatographed with alumina. The least adsorbed material, which had a blue-violet fluorescence in ultraviolet light, after removal of the solvent gave the cyclic sulphone (III) (0·3 g.), m. p. and mixed m.p 195·5—196° (from benzene–light petroleum) (Found : C, 72·5; H, 3·9; S, 11·95%).

Decomposing the diazonium solution in boiling 30% sulphuric acid gave some (III) but the material least adsorbed was fluorescent and yielded *o-chlorophenyl α-naphthyl sulphone* (0·06 g.), needles, m. p. 182·5—183·5° (from alcohol) (Found : C, 63·7; H, 3·6; S, 10·55. $C_{16}H_{11}O_2SCl$ requires C, 63·5; H, 3·7; S, 10·6%). Another experiment gave a minute amount of halogen-free *substance*, m. p. 154·5—155·5, insoluble in aqueous sodium hydroxide and giving no colour with alcoholic ferric chloride (Found : C, 67·1; H, 3·8; S, 10·8. $C_{16}H_{10}O_3S$ requires C, 67·6; H, 4·2; S, 11·3%).

(*b*) *o*-Aminophenyl β-naphthyl sulphone (1·0 g.) was diazotised and treated as described first for the isomer (VI). Repeated chromatography and crystallisation of the product failed to raise the m. p. above 202·5—203° (Found : C, 72·1; H, 3·7; O, 12·2. Calc. for $C_{16}H_{10}O_3S$: C, 72·2; H, 3·8; O, 12·0%). The compound may be a different form of **9-thia-3 : 4-benzofluorene 9 : 9-dioxide** (IV), and a mixture of the two melted at 208°. A hot ethylene glycol solution of this dioxide (IV), when seeded with the crystals of m. p. 202·5—203°, on cooling deposited material of unchanged m. p. (234°). The product from the Pschorr cyclisation was readily reduced with

lithium aluminium hydride to give a good yield of 9-thia-3 : 4-benzofluorene (XVI), m. p. and mixed m. p. 103°.

(*c*) *o*-Aminophenyl phenyl sulphone (1·0 g.) was diazotised and the Pschorr process carried out essentially as above, except that excess of nitrous acid was removed by urea, and the solution was shaken for 1 hr. with 2·0 g. of copper. The precipitated solid, after removal of a small amount of *o*-hydroxy-sulphone (m. p. 82—82·5°) by alkali, gave dibenzothiophen 1 : 1-dioxide (0·2 g.), m. p. 228—229°. In a similar experiment, but where the excess of nitrous acid was not removed, *o-chlorophenyl phenyl sulphone*, (0·58 g.), m. p. 105—105·5°, needles (from benzene), was the main product (Found : C, 57·3; H, 3·6; S, 13·0%). $C_{12}H_9O_2SCl$ requires C, 57·0; H, 3·6; S, 12·7%). *o*-Aminophenyl α-naphthyl sulphide readily gave a diazonium solution which gave only tars on attempted cyclisation with copper powder or sulphuric acid.

Preparation of Polycyclic Sulphones by the Friedel–Crafts Reaction.—Cyclisation of diphenyl-2-sulphonyl chloride. Dibenzothiophen 1 : 1-dioxide (0·05 g.), m. p. 229—230° (from ethanol), was obtained when diphenyl-2-sulphonyl chloride (0·1 g.), tetrachloroethane (5 ml.), and aluminium chloride (0·07 g.) were heated on the water-bath for 30 min., the cooled product was diluted with water (30 ml.), and the tetrachlorethane removed in steam. Cyclisation occurred equally when the mixture was kept at room temperature for 24 hr.

Cyclisation of o-α-naphthylbenzenesulphonyl chloride. This was obtained when powdered potassium *o*-α-naphthylbenzenesulphonate (4·0 g.) (Davies, Gamble, and Savige, *loc. cit.*) and phosphorus pentachloride (2·5 g.) were heated on the water-bath for 1 hr. o-α-*Naphthylbenzenesulphonyl chloride*, precipitated by ice, crystallised from benzene in prisms (2·9 g., 73%), m. p. 136—136·5° (Found : C, 63·5; H, 3·7. $C_{16}H_{11}O_2SCl$ requires C, 63·5; H, 3·6%). This chloride (1·0 g.) and aluminium chloride (0·5 g.) in tetrachloroethane (40 ml.) were kept at room temperature for 24 hr., and after decomposition by cold water (100 ml.) the tetrachloroethane was removed by steam. The residual 3 : 4-benzothiafluorene 9 : 9-dioxide (IV) crystallised from alcohol in needles (0·6 g., 64%), m. p. and mixed m. p. 233—234°.

Preparation of Polycyclic Sulphoxides by the Friedel–Crafts Reaction.—Cyclisation of diphenyl-2-sulphinyl chloride. Crude diphenyl-2-sulphinic acid (0·6 g.) was obtained when diphenyl-2-sulphonyl chloride (0·8 g.) was slowly added to sodium sulphide (1·2 g.) in water (5 ml.), the mixture heated for 1 hr. on the water-bath, and the cold filtered solution acidified with concentrated hydrochloric acid. The sulphinic acid (9·9 g., 77%) was also prepared from 2-aminodiphenyl (10·0 g.) by the Gattermann process as modified by Jenkins and Hambly (*Austral. J. Chem.*, 1953, **6**, 318).

The sulphinic acid, sparingly soluble in cold water, crystallises from aqueous alcohol or aqueous acetone in colourless prisms which rapidly become light yellow; the m. p. varied between 70° and 126°, and a specimen of m. p. 100—124° was analysed (Found : C, 65·0; H, 4·8. Calc. for $C_{12}H_{10}O_2S$: C, 66·1; H, 4·6%). It responds to the usual tests for a sulphinic acid, and its sodium salt (colourless prisms) is sparingly soluble in excess of sodium hydroxide solution. Moreover, the sulphinic acid (0·6 g.) was reoxidised to pure diphenyl-2-sulphonyl chloride (0·53 g., 76%) when shaken for ½ hr. in carbon tetrachloride (20 ml.) containing excess of chlorine : after evaporation, the sulphonyl chloride was recrystallised from light petroleum (b. p. 100—120°).

A solution of freshly prepared diphenyl-2-sulphinic acid (0·25 g.) in ether (10 ml.) was refluxed for 30 min. with thionyl chloride (0·3 ml.), and the ether removed under reduced pressure. Cyclisation of the crude oily diphenyl-2-sulphinyl chloride was achieved by aluminium chloride (0·2 g.) in tetrachloroethane at 0° in 24 hr. The tetrachloroethane solution yielded dibenzothiophen 5-oxide (0·09 g., 51%), needles m. p. 189·5—190° (Courtot and Pomonis, *Compt. rend.*, 1926, **182**, 893, give m. p. 188—188·5°). It was identified by oxidation with hydrogen peroxide in glacial acetic acid to the dioxide, m. p. 229·5—230°. When the cyclisation was done at room temperature, the yield of the sulphoxide fell to 34%.

Cyclisation of o-α-naphthylbenzenesulphinyl chloride. The sulphinic acid (Davies, Gamble, and Savige, *loc. cit.*) (0·75 g.) in ether (25 ml.) was refluxed for 30 min. with thionyl chloride (0·5 ml.). Evaporation gave the oily chloride which was kept with aluminium chloride (0·5 g.) in tetrachloroethane (30 ml.) for 24 hr. at 0°. After steam-distillation the residue was chromatographed in benzene on alumina. The colourless zone with blue fluorescence (ultraviolet) gave colourless prisms, m. p. 147—148° (from benzene–light petroleum), of *9-thia-3 : 4-benzofluorene 9-oxide* (VIII) (Found : C, 77·1; H, 4·2. $C_{16}H_{10}OS$ requires C, 76·8; H, 4·0%). In one experiment a compound less strongly adsorbed on the alumina gave a yellow zone with green fluorescence (ultraviolet), and the eluate gave yellow needles (from benzene–light petroleum), m. p. 120·5—121°, in quantity too small for analysis.

The sulphoxide (VIII) (40 mg.) was refluxed with stannous chloride dihydrate (60 mg.) in alcohol (4 ml.) and concentrated hydrochloric acid for 20 min. and then diluted with water. The product from alcohol (m. p. 102—103°; 28 mg., 71%) was identical (mixed m. p.) with the sulphide (XVI). Oxidation of the sulphoxide with hydrogen peroxide in glacial acetic acid gave the sulphone (IV), as shown by identity of m. p.s.

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NN'-*Diarylthioureas and Related Compounds of Potential Biological Interest.*

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A large number of new *NN'*-diarylthioureas and similar sulphur compounds has been synthesised for testing for tuberculostatic activity and inhibitory properties against influenza virus. The preparation of *p*-alkoxyanilines, aryl *iso*thiocyanates, and a series of aminonaphthaquinones and 1-arylpyrroles was also investigated.

THIOUREA and its derivatives are tuberculostatic. Thiourea itself possesses a slight but definite activity *in vitro*, which is enhanced by appropriate substitution, as in allylthiourea (Jouin and Buu-Hoï, *Ann. Inst. Pasteur*, 1946, **72**, 580), and especially in *p*-aminobenzenesulphonylthiourea (Mayer, *Chem. Abs.*, 1941, **36**, 5199; Jouin and Buu-Hoï, *loc. cit.*), but *NN'*-diarylthioureas failed to reveal significant activity *in vitro*; this group was not therefore investigated further. Interest in these compounds has recently revived with the discovery of outstanding tuberculostatic properties in *NN'*-di-(*p*-*n*-butoxyphenyl)thiourea and related compounds (Mayer, Eisman, and Konopka, *Proc. Soc. Exp. Biol.*, 1953, **82**, 769; Huebner *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 2274), and this activity has been confirmed in a series of new *NN'*-diarylthioureas (Buu-Hoï and Xuong, *Compt. rend.*, 1953, **237**, 498). Further, 4 : 4'-dialkoxythiocarbanilides have been found active against human leprosy (Buu-Hoï, *Internat. J. Leprosy*, 1954, **22**, 16), and certain diarylthioureas and related sulphur compounds against influenza-virus infections in mice (Buu-Hoï, Gley, Xuong, and Bouffanais, *Compt. rend.*, 1954, **238**, 2582).

These findings prompted the preparation of a wide series of new thiourea derivatives for biological testing with regard to these various activities. Some features concerning their preparation are worth mention. Symmetrical *NN'*-diarylthioureas were most conveniently obtained by Hugershof's method (*Ber.*, 1899, **32**, 2246), involving the heating of a primary arylamine with carbon disulphide and sulphur in ethanol. Aryl *iso*thiocyanates used in the preparation of unsymmetrical *NN'*-diarylthioureas were found, at variance with the literature (cf. Guillaumin, "Traité de Chimie organique de Grignard," Masson, Paris, 1939, vol. XIV, p. 348), to be readily accessible by an extension of the Werner reaction (*J.*, 1891, **59**, 399) involving a brief heating of symmetrical *NN'*-diarylthioureas with acetic anhydride. Condensation of the aryl *iso*thiocyanates with a variety of primary arylamines was readily effected in high yields, except in the case of *p*-nitroaniline, which gave no condensation product with aryl *iso*thiocyanates or carbon disulphide under the conditions of the Hugershof reaction. *p*-Aminobenzenesulphonamide, however, readily gave 4 : 4'-disulphonamidothiocarbanilide, a substance briefly mentioned in a patent (Dyson, B.P. 517,682) as being obtained in the reaction of *p*-sulphonamidophenyl *iso*thiocyanate with *p*-aminobenzenesulphonamide; condensation of the last with various aryl *iso*thiocyanates afforded a series of unsymmetrical thioureas bearing the *p*-sulphonamidophenyl radical. An interesting failure of a primary arylamine to condense with aryl *iso*thiocyanates was encountered with *o*-trifluoromethylaniline; this could clearly

be attributed to steric hindrance (cf. Buu-Hoï, Royer, and Hubert-Habart, *Rec. Trav. chim.*, 1954, **73**, 188), as *p*-trifluoromethylaniline readily underwent the reaction. Heterocyclic amines such as aminopyridines and 2-aminothiazole showed the same reactivity as aromatic amines. 2-Aminopyrimidine proved unreactive.

All the thioureas described possess chelating properties towards heavy metals, and most show tuberculostatic activity *in vitro* to some extent; a link between these two properties has been suggested (cf. Buu-Hoï, Xuong, Binon, and Nam, *Compt. rend.*, 1952, **235**, 329). Results of biological tests will be reported elsewhere; one of the most active compounds found was 4-ethyl-4'-*iso*pentyloxythiocarbanilide.

The preparations of several arylamines were improved in the course of this work; their condensation products with 2 : 3-dichloro-1 : 4-naphthaquinone and chloranil (cf. Buu-Hoï, Royer, and Eckert, *Rec. Trav. chim.*, 1952, **71**, 1059), and the 1-aryl-2 : 5-dimethylpyrroles obtained with acetonylacetone (cf. Buu-Hoï, *J.*, 1949, 2882), were prepared for characterisation.

Experimental [with E. Lescot, jun.]

The numerous *products* are tabulated. Unless otherwise stated, those for which no analysis is given are already known; all the others are new. Ligroin had b. p. 100—120°).

Preparation and Characterisation of p-*Alkyl- and* p-*Alkoxy-anilines.*—*p*-Alkylanilines were

Table 1.

(a) *Unsymmetrical substituted thiocarbanilides.*

Thiocarbanilide	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
4-Bromo-4'-fluoro-	177°	$C_{13}H_{10}N_2SBrF$	47·8	3·0	48·0	3·0
4-Bromo-4'-chloro-	202	$C_{13}H_{10}N_2SBrCl$	45·5	2·8	45·6	2·9
4-Bromo-2'-chloro-	198	$C_{13}H_{10}N_2SBrCl$	45·2	3·0	45·6	2·9
4-Bromo-4'-*iso*butoxy-	198	$C_{17}H_{19}ON_2SBr$	53·6	5·2	53·8	5·0
4-Bromo-2' : 5'-dimethoxy-	137	$C_{15}H_{15}O_2N_2SBr$	49·0	4·1	49·0	4·0
4-Bromo-4'-*n*-heptyloxy-	183—184	$C_{20}H_{25}ON_2SBr$	56·8	5·8	57·0	5·9
4-Bromo-4'-dimethylamino-	208	$C_{15}H_{16}N_3SBr$	51·1	4·8	51·4	4·5
4-Bromo-2'-phenyl-	178	$C_{19}H_{15}N_2SBr$	59·3	3·9	59·5	3·9
4-Bromo-4'-hydroxy-	196	$C_{13}H_{11}ON_2SBr$	48·1	3·7	48·2	3·4
4-Ethoxy-4'-methyl-	142	$C_{16}H_{18}ON_2S$	67·0	6·3	67·1	6·2
4-Methoxy-4'-methyl-	161	$C_{15}H_{16}ON_2S$	66·0	6·1	66·1	5·8
4-Methyl-4'-*n*-propoxy-	142	$C_{17}H_{20}ON_2S$	67·7	6·5	68·0	6·6
4-Methyl-4'-*iso*pentyloxy-	135	$C_{19}H_{24}ON_2S$	69·4	7·3	69·5	7·3
4-*iso*Butoxy-4'-methyl-	152	$C_{18}H_{22}ON_2S$	68·5	7·1	68·7	7·0
2-Methoxy-4'-methyl-	149	$C_{15}H_{16}ON_2S$	66·0	6·0	66·1	5·8
2 : 5-Dimethoxy-4'-methyl	128	$C_{16}H_{18}O_2N_2S$	63·7	5·8	63·5	5·9
2-Ethoxy-4'-methyl-	156	$C_{16}H_{18}ON_2S$	67·1	6·3	67·1	6·2
4-*n*-Butoxy-4'-methyl-	139	$C_{18}H_{22}ON_2S$	68·6	7·3	68·7	7·0
4-Methyl-4'-(3-phenylpropoxy)-	130	$C_{23}H_{24}ON_2S$	73·3	6·3	73·4	6·3
4-Ethyl-3'-methyl-	98	$C_{16}H_{18}N_2S$	70·8	6·8	71·1	6·6
2-Ethyl-4'-methyl-	182	$C_{16}H_{18}N_2S$	71·0	6·8	71·1	6·6
4 : 2' : 3'-Trimethyl-	156	$C_{16}H_{18}N_2S$	70·8	6·5	71·1	6·6
4-Methoxy-2' : 3'-dimethyl-	183	$C_{16}H_{18}ON_2S$	66·8	6·0	67·1	6·2
4-Bromo-4'-methoxy-	202	$C_{14}H_{13}ON_2SBr$	49·7	3·9	49·8	3·8
2-Chloro-4'-methoxy-	173	$C_{14}H_{13}ON_2SCl$	57·2	4·5	57·4	4·4
4-Fluoro-4'-methoxy-	172	$C_{14}H_{13}ON_2SF$	60·8	5·0	60·8	4·7
2 : 4'-Dimethoxy-	161	$C_{15}H_{16}O_2N_2S$	62·2	5·4	62·4	5·5
2-Ethoxy-4'-methoxy-	157	$C_{16}H_{18}O_2N_2S$	63·3	6·1	63·5	5·9
4 : 2' : 5'-Trimethoxy-	149	$C_{16}H_{18}O_2N_2S$	60·0	5·8	60·3	5·6
4-Arsono-4'-methyl-	d. *ca.* 262 *	$C_{14}H_{15}O_3N_2SAs$	45·4	3·8	45·9	4·0
4-Hydroxy-4'-methoxy-	198	$C_{14}H_{14}O_2N_2S$	61·1	5·2	61·3	5·1
4-Butoxy-4'-methoxy-	164	$C_{18}H_{22}O_2N_2S$	65·1	6·6	65·4	6·6
4-*iso*Butoxy-4'-methoxy-	161	$C_{18}H_{22}O_2N_2S$	65·6	6·5	65·4	6·6
4-Methoxy-4'-*iso*pentyloxy-	155	$C_{19}H_{24}O_2N_2S$	66·1	7·0	66·2	6·9
4-Methoxy-4'-(3-phenylpropoxy)-	154	$C_{23}H_{24}O_2N_2S$	70·5	6·4	70·4	6·1
4-Ethoxy-2' : 5'-dimethoxy-	149	$C_{17}H_{20}O_2N_2S$	61·3	6·2	61·4	6·0
4-Ethoxy-2'-methoxy-	129	$C_{16}H_{18}O_2N_2S$	63·4	6·0	63·5	5·9
4-Ethoxy-4'-(3-phenylpropoxy)-	147	$C_{24}H_{26}O_2N_2S$	70·6	6·6	70·9	6·4
4-Ethoxy-4'-hydroxy-	196	$C_{15}H_{16}O_2N_2S$	62·3	5·8	62·4	5·5
2-Chloro-4'-ethoxy-	191	$C_{15}H_{15}ON_2SCl$	58·4	5·0	58·7	4·8
4-Ethoxy-3' : 4'-dimethyl-	122	$C_{17}H_{20}ON_2S$	68·1	6·9	68·0	6·6

* d. = decomp.

TABLE 1. (*Continued.*)

Thiocarbanilide	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
3-Chloro-4′-ethoxy-	133°	$C_{15}H_{15}ON_2SCl$	58·8	4·8	58·7	4·8
4-Bromo-4′-ethoxy-	179	$C_{15}H_{15}ON_2SBr$	51·1	4·1	51·2	4·2
4-Dimethylamino-4′-ethoxy-	197	$C_{17}H_{21}ON_3S$	64·4	6·5	64·7	6·6
4-Ethoxy-4′-fluoro-	172	$C_{15}H_{15}ON_2SF$	62·0	5·4	62·0	5·1
4-Chloro-4′-ethoxy-	189	$C_{15}H_{15}ON_2SCl$	58·3	5·0	58·7	4·8
4-Ethoxy-2′-phenyl-	144	$C_{21}H_{20}ON_2S$	72·3	6·0	72·4	5·7
4 : 3′ : 4′-Trimethyl-	134	$C_{16}H_{16}N_2S$	71·0	6·5	71·1	6·6
2-Chloro-4′-methyl-	184	$C_{14}H_{12}N_2SCl$	60·5	4·8	60·7	4·7
3-Chloro-4′-methyl-	138	$C_{14}H_{12}N_2SCl$	60·4	4·7	60·7	4·7
4-*n*-Heptyloxy-2′ : 4′-dimethyl-	124	$C_{22}H_{30}ON_2S$	71·1	8·2	71·3	8·1
4-Dimethylamino-2′ : 4′-dimethyl-	155	$C_{17}H_{21}N_3S$	68·0	7·3	68·2	7·0
2 : 4-Dimethyl-4′-(3-phenylpropoxy)-	115	$C_{24}H_{26}ON_2S$	73·6	6·6	73·8	6·6
4-Fluoro-2′ : 4′-dimethyl-	131	$C_{15}H_{15}N_2SF$	65·6	5·5	65·5	5·4
2-*tert.*-Butyl-	190	$C_{17}H_{20}N_2S$	71·5	7·1	71·8	7·0
2-*tert.*-Butyl-2′-ethoxy-	172	$C_{19}H_{24}ON_2S$	69·6	7·5	69·5	7·3
4-Bromo-2-*tert.*-butyl-	187	$C_{17}H_{19}N_2SBr$	56·0	5·5	56·1	5·2
4-Fluoro-4′-hydroxy-	179	$C_{13}H_{11}ON_2SF$	59·4	4·1	59·5	4·1
4-Fluoro-3′-methyl-	125	$C_{14}H_{13}N_2SF$	64·5	5·1	64·6	5·0
4-Fluoro-2′-phenyl-	163	$C_{19}H_{15}N_2SF$	70·5	4·6	70·8	4·6
4-Methyl-4′-sulphonamido-	234	$C_{14}H_{15}O_2N_3S_2$	52·2	4·5	52·3	4·6
2-Chloro-4′-fluoro-	189	$C_{13}H_{10}N_2SClF$	55·3	3·6	55·6	3·5
4-*iso*Butoxy-4′-fluoro-	179	$C_{17}H_{19}ON_2SF$	64·0	5·9	64·1	5·9
3-Chloro-4′-fluoro-	136	$C_{12}H_{10}N_2SClF$	55·3	3·3	55·6	3·5
4-Dimethylamino-4′-fluoro-	193—194	$C_{15}H_{16}N_3SF$	62·4	5·4	62·2	5·5
4-Chloro-4′-fluoro-	169	$C_{13}H_{10}N_2SClF$	55·5	3·8	55·6	3·5
4-Fluoro-2′ : 5′-dimethoxy-	161	$C_{15}H_{15}O_2N_2SF$	58·6	5·0	58·8	4·9
4-Fluoro-4′-*n*-heptyloxy-	162	$C_{20}H_{25}ON_2SF$	66·3	7·1	66·6	6·9
4-Fluoro-4′-(3-phenylpropoxy)-	139	$C_{23}H_{21}ON_2SF$	69·2	5·3	69·4	5·5
4-Chloro-4′-*n*-propoxy-	189	$C_{16}H_{17}ON_2SCl$	59·8	5·4	60·0	5·3
4-(3-Phenylpropoxy)-4′-*n*-propoxy-	143	$C_{25}H_{28}O_2N_2S$	71·3	6·8	71·4	6·6
4-Fluoro-4′-*n*-propoxy-	178	$C_{16}H_{17}ON_2SF$	63·0	5·4	63·1	5·5
4-Dimethylamino-4-*n*-propoxy-	156	$C_{18}H_{22}ON_3S$	65·3	7·1	65·6	6·9
4-Hydroxy-4′-*n*-propoxy-	198	$C_{16}H_{18}O_2N_2S$	63·8	5·8	63·5	5·9
4-*iso*Butoxy-4′-*n*-propoxy-	175	$C_{20}H_{26}O_2N_2S$	67·0	7·2	67·0	7·2
4-*n*-Pentyloxy-4′-*n*-propoxy-	167	$C_{21}H_{28}O_2N_2S$	67·4	7·4	67·7	7·5
4-*n*-Heptyloxy-4′-*n*-propoxy-	162	$C_{23}H_{32}O_2N_2S$	68·8	8·2	69·0	8·0
4-Bromo-4′-*n*-butoxy-	189	$C_{17}H_{19}ON_2SBr$	53·5	5·0	53·8	5·0
4-*n*-Butoxy-4′-fluoro-	168	$C_{17}H_{19}ON_2SF$	64·0	6·0	64·1	5·9
4-*n*-Butoxy-4′-(3-phenylpropoxy)-	149	$C_{26}H_{30}O_2N_2S$	72·0	6·8	71·8	6·9
4-*n*-Butoxy-4′-hydroxy-	186	$C_{17}H_{20}O_2N_2S$	64·2	6·4	64·5	6·3
4-*n*-Butoxy-4′-trifluoromethyl-	186	$C_{18}H_{19}ON_2SF_3$	58·5	5·1	58·6	5·1
4-Chloro-4′-*iso*pentyloxy-	186	$C_{18}H_{21}ON_2SCl$	62·0	6·1	61·9	6·0
4-Fluoro-4′-*iso*pentyloxy-	171	$C_{18}H_{21}ON_2SF$	64·7	6·4	65·0	6·3
4-*n*-Heptyloxy-4′-*iso*pentyloxy-	121	$C_{25}H_{36}O_2N_2S$	69·8	8·2	70·0	8·4
4-*iso*Pentyloxy-4′-(3-phenylpropoxy)-	132	$C_{27}H_{32}O_2N_2S$	72·0	7·2	72·3	7·1
4-Hydroxy-4′-*iso*pentyloxy-	158	$C_{18}H_{22}O_2N_2S$	65·3	6·5	65·4	6·6
4-Hydroxy-4′-*n*-pentyloxy-	172	$C_{18}H_{22}O_2N_2S$	65·1	6·5	65·4	6·6
4-Dimethylamino-4′-*n*-pentyloxy-	142	$C_{20}H_{27}ON_3S$	67·0	7·8	67·2	7·5
4-*iso*Butoxy-4′-*n*-pentyloxy-	143	$C_{22}H_{30}O_2N_2S$	68·0	7·5	68·3	7·7
4-Chloro-4′-*n*-pentyloxy-	172	$C_{18}H_{21}ON_2SCl$	61·7	6·3	61·9	6·0
4-Fluoro-4′-*n*-pentyloxy-	168	$C_{18}H_{21}ON_2SF$	64·8	6·1	65·0	6·3
4-*iso*Butoxy-2′-phenyl-	145	$C_{22}H_{24}ON_2S$	73·5	6·5	73·4	6·3
4-Dimethylamino-2′-phenyl-	174	$C_{21}H_{21}N_3S$	72·3	6·1	72·6	6·0
4-Hydroxy-2′-phenyl-	168	$C_{19}H_{16}ON_2S$	70·9	5·1	71·2	5·0
4-Chloro-2′-phenyl-	191	$C_{19}H_{15}N_2SCl$	67·0	4·5	67·3	4·4
4-*n*-Heptyloxy-2′-phenyl-	123	$C_{26}H_{30}ON_2S$	74·7	7·4	74·6	7·1
2-Phenyl-4′-(3-phenylpropoxy)-	131	$C_{28}H_{26}ON_2S$	76·7	6·0	76·7	5·9
4-Fluoro-	194	$C_{13}H_{11}N_2SF$	63·2	4·5	63·4	4·4
4-Fluoro-4′-methyl-	179	$C_{14}H_{13}N_2SF$	64·5	5·0	64·6	5·0
4-Fluoro-2′-methoxy-	121	$C_{14}H_{13}ON_2SF$	61·0	5·0	60·8	4·7
2-Ethoxy-4′-fluoro-	134	$C_{15}H_{15}ON_2SF$	62·0	5·2	62·0	5·1
4-Ethyl-	129	$C_{15}H_{16}N_2S$	70·2	6·5	70·3	6·2
4-Ethyl-4′-methyl-	155	$C_{16}H_{18}N_2S$	71·3	6·5	71·1	6·6
4-Ethyl-4′-methoxy-	163	$C_{16}H_{18}ON_2S$	67·0	6·2	67·1	6·2
4-Ethoxy-4′-ethyl-	158	$C_{17}H_{20}ON_2S$	67·8	6·9	68·0	6·6
2-Ethoxy-4′-ethyl-	148	$C_{17}H_{20}ON_2S$	67·8	6·6	68·0	6·6
4-Ethyl-4′-*iso*pentyloxy-	138	$C_{20}H_{26}ON_2S$	70·0	7·6	70·1	7·6
4-Bromo-4′-ethyl-	198	$C_{15}H_{15}N_2SBr$	53·3	4·3	53·7	4·4
4-Ethyl-2′ : 4′-dimethyl-	119	$C_{17}H_{20}N_2S$	71·5	7·2	71·8	7·0
4-Ethyl-2′ : 3′-dimethyl-	172	$C_{17}H_{20}N_2S$	71·8	7·3	71·8	7·0
4-Ethyl-4′-*n*-propoxy-	154	$C_{18}H_{22}ON_2S$	68·5	7·1	68·7	7·0

TABLE 1. (*Continued.*)

Thiocarbanilide	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
4-Ethyl-4'-*iso*propoxy-	134°	$C_{18}H_{22}ON_2S$	68·5	7·3	68·7	7·0
4-Bromo-3'-fluoro-6'-methoxy-	152	$C_{14}H_{12}ON_2SBrF$	47·0	3·1	47·3	3·3
4-*n*-Butoxy-4'-ethyl-	144	$C_{19}H_{24}ON_2S$	69·5	7·2	69·5	7·3
4-*iso*Butoxy-4'-ethyl-	146	$C_{19}H_{24}ON_2S$	69·6	7·6	69·5	7·3
4-Ethyl-4'-fluoro-	168	$C_{15}H_{15}N_2SF$	65·4	5·4	65·6	5·4
4-Chloro-4'-ethyl-	197	$C_{15}H_{15}N_2SCl$	61·6	5·2	61·9	5·1
4-*n*-Propyl-	126	$C_{16}H_{16}N_2S$	71·0	6·6	71·1	6·6
4-Methyl-4'-*n*-propyl-	131	$C_{17}H_{20}N_2S$	71·6	7·0	71·8	7·0
4-Methoxy-4'-*n*-propyl-	164	$C_{17}H_{20}ON_2S$	67·9	6·6	68·0	6·6
4-Methoxy-4'-sulphonamido-	232—234	$C_{14}H_{15}O_3N_3S_2$	49·5	4·2	49·8	4·4
2-Methoxy-4'-*n*-propyl-	129	$C_{17}H_{20}ON_2S$	68·1	6·5	68·0	6·6
4-Ethoxy-4'-*n*-propyl-	166	$C_{18}H_{22}ON_2S$	68·5	7·1	68·7	7·0
2-Ethoxy-4'-*n*-propyl-	161	$C_{18}H_{22}ON_2S$	68·4	7·2	68·7	7·0
4-*iso*Pentyloxy-4'-*n*-propyl-	138	$C_{21}H_{28}ON_2S$	70·8	8·0	70·7	7·8
4-Bromo-4'-*n*-propyl-	187	$C_{16}H_{17}N_2SBr$	54·7	5·0	55·0	4·8
2 : 4-Dimethyl-4'-*n*-propyl-	129	$C_{18}H_{22}N_2S$	72·6	7·5	72·4	7·3
2-Phenyl-4'-*n*-propyl-	143	$C_{22}H_{22}N_2S$	76·5	6·2	76·3	6·3
4-*n*-Propoxy-4'-*n*-propyl-	168	$C_{19}H_{24}ON_2S$	69·6	7·6	69·5	7·3
4-*iso*Propoxy-4'-*n*-propyl-	155	$C_{19}H_{24}ON_2S$	69·4	7·5	69·5	7·3
4-*n*-Butoxy-4'-*n*-propyl-	157	$C_{20}H_{26}ON_2S$	70·0	7·5	70·1	7·6
4-*iso*Butoxy-4'-*n*-propyl-	159	$C_{20}H_{26}ON_2S$	70·2	7·6	70·1	7·6
4-Fluoro-4'-*n*-propyl-	157	$C_{16}H_{17}N_2SF$	66·6	6·0	66·6	5·9
4-Chloro-4'-*n*-propyl-	177	$C_{16}H_{17}N_2SCl$	62·8	5·5	63·0	5·5
4-*n*-Butyl-	144	$C_{17}H_{20}N_2S$	71·7	7·2	71·8	7·0
4-*n*-Butyl-4'-methyl-	137	$C_{18}H_{22}N_2S$	72·3	7·5	72·4	7·3
4-*n*-Butyl-4'-methoxy-	169	$C_{18}H_{22}ON_2S$	68·4	7·1	68·7	7·0
4-*n*-Butyl-2'-methoxy-	121	$C_{18}H_{22}ON_2S$	68·5	7·2	68·7	7·0
4-*n*-Butyl-4'-ethoxy-	159	$C_{19}H_{24}ON_2S$	69·4	7·2	69·5	7·3
4-*n*-Butyl-2'-ethoxy-	138	$C_{19}H_{24}ON_2S$	69·2	7·1	69·5	7·3
4-*n*-Butyl-4'-*iso*pentyloxy-	132	$C_{22}H_{30}ON_2S$	71·3	8·2	71·3	8·1
4-*n*-Butyl-4'-*n*-propoxy-	167	$C_{20}H_{26}ON_2S$	70·2	7·6	70·1	7·6
4-*n*-Butyl-4'-*iso*propoxy-	138	$C_{20}H_{26}ON_2S$	70·2	7·8	70·1	7·6
4-*n*-Butoxy-4'-*n*-butyl-	161	$C_{21}H_{28}ON_2S$	70·4	7·9	70·7	7·8
4-*iso*Butoxy-4'-*n*-butyl-	151	$C_{21}H_{28}ON_2S$	70·7	7·8	70·7	7·8
4-*n*-Butyl-4'-fluoro-	162	$C_{17}H_{19}N_2SF$	67·4	6·4	67·5	6·2
4-*n*-Butyl-4'-chloro-	174	$C_{17}H_{19}N_2SCl$	64·2	5·8	64·0	5·9
4-Bromo-4'-*n*-butyl-	181	$C_{17}H_{19}N_2SBr$	56·0	5·0	56·1	5·2
4-Fluoro-4'-*n*-heptyl-	158	$C_{26}H_{33}N_2SF$	69·5	7·5	69·7	7·2
4-Chloro-4'-*n*-heptyl-	167	$C_{20}H_{33}N_2SCl$	66·3	6·8	66·5	6·9
4-Bromo-4'-*n*-heptyl-	176	$C_{20}H_{33}N_2SBr$	59·4	6·1	59·2	6·1
4-Ethoxy-4'-sulphonamido*	246	$C_{15}H_{17}O_3N_3S_2$	—	—	—	—
4-*n*-Heptyl-4'-methyl	129	$C_{21}H_{28}N_2S$	74·0	8·5	74·1	8·2
4-Ethoxy-4'-*n*-heptyl-	151	$C_{22}H_{30}ON_2S$	71·3	8·3	71·3	8·1
4-*n*-Heptyl-4'-*n*-propoxy-	156	$C_{23}H_{32}ON_2S$	71·7	7·9	71·8	8·0
4-*n*-Heptyl-4'-*iso*propoxy-	136	$C_{23}H_{32}ON_2S$	71·6	8·0	71·8	8·0
4-*n*-Butoxy-4'-*n*-heptyl-	151	$C_{24}H_{34}ON_2S$	72·5	8·5	72·3	8·5
4-*iso*Butoxy-4'-*n*-heptyl-	116	$C_{24}H_{34}ON_2S$	72·2	8·6	72·3	8·5
4-*n*-Heptyl-4'-*iso*pentyloxy-	112	$C_{25}H_{36}ON_2S$	72·9	8·7	72·8	8·4
4-Ethyl-4'-*n*-propyl-	139	$C_{18}H_{22}N_2S$	72·3	7·5	72·4	7·3
4-*n*-Butyl-4'-*n*-propyl-	164	$C_{20}H_{26}N_2S$	73·5	8·0	73·6	7·9
4-*n*-Heptyl-4'-*n*-propyl-	138	$C_{23}H_{32}N_2S$	74·7	8·8	75·0	8·6
4-*n*-Butyl-4'-ethyl-	138	$C_{19}H_{24}N_2S$	72·9	7·9	73·0	7·6
4-*n*-Butyl-4'-*n*-heptyl-	140	$C_{24}H_{34}N_2S$	75·4	8·9	75·3	8·8
2-Methylthio-	189	$C_{14}H_{14}N_2S_2$	61·5	5·0	61·2	5·1
4-Methyl-2'-methylthio-	204	$C_{15}H_{16}N_2S_2$	62·6	5·8	62·5	5·5
3-Methyl-2'-methylthio-	174	$C_{15}H_{16}N_2S_2$	62·4	5·6	62·5	5·5
2-Methylthio-4'-*n*-propyl-	183	$C_{17}H_{20}N_2S_2$	64·3	6·2	64·5	6·3
4-*n*-Butyl-2'-methylthio-	179	$C_{18}H_{22}N_2S_2$	65·1	6·6	65·4	6·6
4-Ethoxy-2'-methylthio-	202	$C_{16}H_{16}ON_2S_2$	60·0	5·5	60·3	5·6
2-Methylthio-4'-*n*-propoxy-	204	$C_{17}H_{20}ON_2S_2$	61·3	6·2	61·4	6·0
2-Methylthio-4'-*iso*propoxy-	144	$C_{17}H_{20}ON_2S_2$	61·2	6·1	61·4	6·0
4-*n*-Butoxy-2'-methylthio-	194	$C_{18}H_{22}ON_2S_2$	62·1	6·3	62·4	6·3
4-*iso*Butoxy-2'-methylthio-	207	$C_{18}H_{22}ON_2S_2$	62·2	6·2	62·4	6·3
2-Methylthio-4'-*iso*pentyloxy-	189	$C_{19}H_{24}ON_2S_2$	63·0	6·9	63·3	6·6
4-Fluoro-2'-methylthio-	217	$C_{14}H_{13}N_2S_2F$	57·2	4·6	57·5	4·4
4-Chloro-2'-methylthio-	225	$C_{14}H_{13}N_2S_2Cl$	54·1	4·2	54·4	4·2
4-Bromo-2'-methylthio-	228	$C_{14}H_{13}N_2S_2Br$	47·5	3·8	47·5	3·6
2-Methylseleno-	196	$C_{14}H_{14}N_2SSe$	52·1	4·1	52·3	4·3

* No m. p. available in the literature for this compound (Ganapathi, *J. Indian Chem. Soc.*, 1938, **15**, 255; *Proc. Indian Acad. Sci.*, 1940, **11**, *A*, 298).

TABLE 1. (*Continued.*)

Thiocarbanilide	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
4-Methyl-2′-methylseleno-	209°	$C_{15}H_{16}N_2SSe$	53·4	4·7	53·7	4·7
3-Methyl-2′-methylseleno-	176	$C_{15}H_{16}N_2SSe$	53·6	4·6	53·7	4·7
2-Methylseleno-4′-*n*-propyl-	182	$C_{17}H_{20}N_2SSe$	56·0	5·8	56·2	5·5
4-*n*-Butyl-2′-methylseleno-	178	$C_{18}H_{22}N_2SSe$	57·0	5·8	57·2	5·8
4-Ethoxy-2′-methylseleno-	207	$C_{16}H_{16}ON_2SSe$	52·5	5·2	52·6	4·9
2-Methylseleno-4′-*n*-propoxy-	203	$C_{17}H_{20}ON_2SSe$	53·5	5·1	53·8	5·2
2-Methylseleno-4′-*iso*propoxy-	151	$C_{17}H_{20}ON_2SSe$	53·7	5·3	53·8	5·2
4-*n*-Butoxy-2′-methylseleno-	195	$C_{18}H_{22}ON_2SSe$	54·6	5·8	54·9	5·5
4-*iso*Butoxy-2′-methylseleno-	198	$C_{18}H_{22}ON_2SSe$	54·8	5·8	54·9	5·5
2-Methylseleno-4′-*iso*pentyloxy-	189	$C_{19}H_{24}ON_2SSe$	56·2	5·7	56·0	5·8
4-Fluoro-2′-methylseleno-	221	$C_{14}H_{13}N_2SSeF$	49·2	4·1	49·5	3·8
4-Chloro-2′-methylseleno-	226	$C_{14}H_{13}N_2SSeCl$	47·0	3·5	47·2	3·6
4-Bromo-2′-methylseleno-	232	$C_{14}H_{13}N_2SSeBr$	41·7	3·1	42·0	3·2
4-Chloro-4′-fluoro-6-methoxy-	139	$C_{14}H_{12}ON_2SFCl$	53·8	4·0	54·1	3·8
4-Chloro-4′-fluoro-5′-methyl-	181	$C_{14}H_{12}N_2SFCl$	56·7	4·1	57·0	4·0
4-Chloro-5′-fluoro-4′-methoxy-	179	$C_{14}H_{12}ON_2SFCl$	54·0	4·1	54·1	3·8
3-Fluoro-6-methoxy-4′-methyl-	148	$C_{15}H_{15}ON_2SF$	62·2	5·2	62·0	5·1
4-Ethoxy-3′-fluoro-6′-methoxy-	163	$C_{16}H_{17}O_2N_2SF$	60·1	5·5	60·0	5·3
3-Fluoro-6-methoxy-4′-*iso*pentyloxy-	93	$C_{19}H_{23}O_2N_2SF$	63·2	6·1	62·9	6·3
4-Phenyl-	208	$C_{19}H_{16}N_2S$	75·2	5·5	75·0	5·2
4-Fluoro-4′-phenyl-	221	$C_{19}H_{15}N_2SF$	71·0	4·5	70·8	4·6
4-Bromo-4′-phenyl-	229	$C_{19}H_{15}N_2SBr$	59·2	4·0	59·5	3·9
4-*n*-Heptyl-4′-phenyl-	219	$C_{26}H_{36}N_2S$	77·5	7·4	77·6	7·4
4-Methoxy-4′-phenyl-	211	$C_{20}H_{18}ON_2S$	71·5	5·5	71·8	5·3
2-Methoxy-4′-phenyl-	223	$C_{20}H_{18}ON_2S$	71·6	5·6	71·8	5·3
4-Ethoxy-4′-phenyl-	226	$C_{21}H_{20}ON_2S$	72·3	5·5	72·4	5·7
2-Ethoxy-4′-phenyl-	232	$C_{21}H_{20}ON_2S$	72·1	5·9	72·4	5·7
4-*iso*Butoxy-4′-phenyl-	225	$C_{23}H_{24}ON_2S$	73·2	6·2	73·4	6·3
4-*iso*Pentyloxy-4′-phenyl-	195	$C_{24}H_{26}ON_2S$	74·1	6·5	73·8	6·6
2 : 4′-Diphenyl-	226	$C_{25}H_{20}N_2S$	78·8	5·4	78·9	5·2
2 : 5-Dichloro-	177	$C_{13}H_{10}N_2SCl_2$	52·2	3·4	52·5	3·3
2 : 5-Dichloro-4′-fluoro-	174	$C_{13}H_9N_2SFCl_2$	49·4	3·0	49·5	2·8
2 : 5-Dichloro-4′-chloro-	201	$C_{13}H_9N_2SCl_3$	46·8	2·9	47·0	2·7
4-Bromo-2′ : 5′-dichloro-	193	$C_{13}H_9N_2SCl_2Br$	41·1	2·2	41·4	2·3
2 : 5-Dichloro-4′-methyl-	162	$C_{14}H_{12}N_2SCl_2$	54·2	3·8	54·0	3·8
2 : 5-Dichloro-3′-methyl-	156	$C_{14}H_{12}N_2SCl_2$	53·7	3·6	54·0	3·8
2 : 5-Dichloro-4′-methoxy-	177	$C_{14}H_{12}ON_2SCl_2$	51·0	3·5	51·3	3·6
2 : 5-Dichloro-2′-methoxy-	154	$C_{14}H_{12}ON_2SCl_2$	51·2	3·6	51·3	3·6
2 : 5-Dichloro-4′-ethoxy-	172	$C_{15}H_{14}ON_2SCl_2$	52·8	4·3	52·7	4·1
2 : 5-Dichloro-4′-*n*-propoxy-	158	$C_{16}H_{16}ON_2SCl_2$	53·7	4·4	54·0	4·5
2 : 5-Dichloro-4′-*iso*propoxy-	151	$C_{16}H_{16}ON_2SCl_2$	54·1	4·3	54·0	4·5
4-*n*-Butoxy-2′ : 5′-dichloro-	145	$C_{17}H_{18}ON_2SCl_2$	55·0	5·0	55·2	4·8
4-*iso*Butoxy-2′ : 5′-dichloro-	161	$C_{17}H_{18}ON_2SCl_2$	55·1	4·6	55·2	4·8
2-Methoxy-5-methyl-	181	$C_{15}H_{16}ON_2S$	66·2	5·6	66·1	5·8
2-Methoxy-4′-fluoro-5-methyl-	142	$C_{15}H_{15}ON_2SF$	62·2	5·2	62·0	5·1
4-Chloro-2′-methoxy-5′-methyl-	153	$C_{15}H_{15}ON_2SCl$	58·4	4·9	58·7	4·8
4-Bromo-2′-methoxy-5′-methyl-	161	$C_{15}H_{15}ON_2SBr$	51·0	4·4	51·2	4·2
2-Methoxy-5 : 4′-dimethyl-	139	$C_{16}H_{18}ON_2S$	67·0	6·3	67·1	6·2
2-Methoxy-5 : 3′-dimethyl-	129	$C_{16}H_{18}ON_2S$	67·3	6·1	67·1	6·2
(b) Symmetrical substituted thiocarbanilides.						
4 : 4′-Dichloro-2 : 2′-dimethoxy-	151—152°	$C_{15}H_{14}O_2N_2SCl_2$	50·3	4·0	50·4	3·9
2 : 3 : 2′ : 3′-Tetramethyl-	224	$C_{17}H_{20}N_2S$	71·5	7·3	71·8	7·0
4 : 4′-Di-*n*-heptyloxy-	155	$C_{27}H_{40}O_2N_2S$	71·1	8·9	71·0	8·7
2 : 2′-Diethoxy-	126	$C_{17}H_{20}O_2N_2S$	64·3	6·3	64·5	6·3
4 : 4′-Di-(3-phenylpropyloxy)-	159—160	$C_{31}H_{32}O_2N_2S$	75·1	6·3	75·0	6·4
2 : 2′-Diphenyl-	165—166	$C_{25}H_{20}N_2S$	79·1	5·5	78·9	5·2
4 : 4′-Di-*n*-propyl-	154	$C_{19}H_{24}N_2S$	—	—	—	—
4 : 4′-Di-*n*-butyl-	159	$C_{21}H_{28}N_2S$	—	—	—	—
4 : 4′-Di-*n*-heptyl-	152	$C_{27}H_{40}N_2S$	76·3	9·4	76·4	9·4
2 : 2′-Dimethylthio-	159	$C_{15}H_{16}H_2S_3$	56·0	5·3	56·2	5·0
2 : 2′-Dimethylseleno-	167	$C_{15}H_{16}N_2Se_2$	47·3	4·2	47·6	4·1
4 : 4′-Di*iso*propoxy-	142	$C_{19}H_{24}O_2N_2S$	66·3	7·1	66·2	6·9
2 : 2′-Di-*tert.*-butyl-	182	$C_{21}H_{28}N_2S$	74·3	8·3	74·1	8·2
4 : 4′-Disulphonamido-	d. *ca.* 248 *	$C_{13}H_{14}O_4N_4S_3$	—	—	—	—
2 : 2′-Dimethoxy-5 : 5′-dimethyl-	146	$C_{17}H_{20}O_2N_2S$	64·2	6·1	64·5	6·3
4 : 4′-Difluoro-	208	$C_{13}H_{10}N_2SF_2$	59·0	3·6	59·1	3·8
3 : 3′ : 4 : 4′-Tetrachloro-	180—181	$C_{13}H_8N_2SCl_4$	42·3	2·2	42·6	2·1

* Dyson, George, and Hunter (*J.*, 1926, 3042) gave m. p. 144°.

prepared free from *o*- and *m*-isomers by Beckmann rearrangement of the appropriate 4-alkylacetophenone oximes, and hydrolysis of the resulting *p*-alkylacetanilides. *p*-*n*-Propylaniline thus obtained had b. p. 229°, n_D^{22} 1·5428; the product prepared by alkylating aniline with *n*-propyl alcohol and zinc chloride (Francksen, *Ber.*, 1884, **17**, 1221) must have been impure, as the 4 : 4'-di-*n*-propylthiocarbanilide derived from it was reported to melt at 138°, whereas a pure sample was now found to melt at 154°. Pure *p*-*n*-butylaniline had b. p. 242°, n_D^{23} 1·5361; Reilly and Hickinbottom (*J.*, 1918, **113**, 983) gave b. p. 258—260°/750 mm. p-n-*Heptylaniline* was a pale yellow oil, b. p. 286°, n_D^{23} 1·5205 (Found: C, 81·5; H, 11·3. $C_{13}H_{31}N$ requires C, 81·7; H, 11·0%); Auger (*Bull. Soc. chim. France*, 1887, **47**, 50) gave b. p. 175°/10 mm. for an amine prepared by reduction of a nitro-*n*-heptylbenzene of unknown constitution.

TABLE 2. NN'-*Disubstituted thioureas*, R·NH·CS·NHR'.

R'	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
R = 1-$C_{10}H_7$.						
p-Fluorophenyl-	185°	$C_{17}H_{13}N_2SF$	68·6	4·1	68·9	4·3
p-Chlorophenyl	192	$C_{17}H_{13}N_2SCl$	65·0	4·3	65·2	4·1
m-Chlorophenyl-	156	$C_{17}H_{13}N_2SCl$	65·1	4·1	65·2	4·1
2 : 5-Dichlorophenyl-	202	$C_{17}H_{12}N_2SCl_2$	58·3	3·4	58·7	3·4
3 : 4-Dichlorophenyl-	191	$C_{17}H_{12}N_2SCl_2$	58·5	3·5	58·7	3·4
p-Bromophenyl-	226	$C_{17}H_{13}N_2SBr$	56·3	3·5	56·6	3·6
p-Tolyl-	204	$C_{18}H_{16}N_2S$	74·0	5·5	73·9	5·4
2 : 4-Dimethylphenyl-	189	$C_{19}H_{18}N_2S$	74·7	6·0	74·5	5·8
p-Ethylphenyl-	173	$C_{19}H_{18}N_2S$	74·3	6·0	74·5	5·8
n-Propylphenyl-	168	$C_{20}H_{20}N_2S$	74·8	6·1	75·0	6·2
n-Butylphenyl-	164	$C_{21}H_{22}N_2S$	75·5	6·5	75·4	6·5
p-*n*-Heptylphenyl-	149	$C_{24}H_{28}N_2S$	76·5	7·6	76·5	7·4
p-Hydroxyphenyl-	208	$C_{17}H_{14}ON_2S$	69·0	4·8	69·3	4·7
p-Methoxyphenyl-	194	$C_{18}H_{16}ON_2S$	70·0	5·2	70·1	5·1
3-Fluoro-6-methoxyphenyl-	137	$C_{18}H_{15}ON_2SF$	66·0	4·8	66·2	4·6
2 : 5-Dimethoxyphenyl-	153	$C_{19}H_{18}O_2N_2S$	67·1	5·2	67·4	5·3
p-Phenetyl-	201	$C_{19}H_{18}ON_2S$	70·7	5·5	70·8	5·5
o-Phenetyl-	164	$C_{19}H_{18}ON_2S$	70·5	5·6	70·8	5·5
p-*n*-Butoxyphenyl-	157	$C_{21}H_{22}ON_2S$	72·2	6·5	72·0	6·2
p-*iso*Butoxyphenyl-	166	$C_{21}H_{22}ON_2S$	72·0	6·1	72·0	6·2
p-*iso*Pentyloxyphenyl-	163	$C_{22}H_{24}ON_2S$	72·3	6·8	72·2	6·5
p-3-Phenylpropoxyphenyl-	152	$C_{26}H_{24}ON_2S$	75·6	5·9	75·7	5·8
o-Methylthiophenyl-	178	$C_{18}H_{16}N_2S_2$	66·3	4·9	66·6	4·9
o-Methylselenophenyl-	174	$C_{18}H_{16}N_2SSe$	58·8	4·4	59·1	4·3
p-Dimethylaminophenyl-	189	$C_{19}H_{19}N_3S$	70·8	6·1	71·0	5·9
2-Naphthyl-	201	$C_{21}H_{16}N_2S$	76·5	5·0	76·8	4·8
5-Hydroxy-1-naphthyl-	219	$C_{21}H_{16}ON_2S$	73·0	4·5	73·2	4·6
4-Chloro-1-naphthyl-	212	$C_{21}H_{15}N_2SCl$	69·2	4·1	69·5	4·1
R = 2-$C_{10}H_7$.						
p-Fluorophenyl-	203	$C_{17}H_{13}N_2SF$	68·6	4·2	68·9	4·3
p-Chlorophenyl-	215	$C_{17}H_{13}N_2SCl$	65·0	4·2	65·2	4·1
2 : 5-Dichlorophenyl-	179	$C_{17}H_{12}N_2SCl_2$	58·7	3·7	58·7	3·4
p-Bromophenyl-	212	$C_{17}H_{12}N_2SBr$	56·3	3·6	56·6	3·6
p-Tolyl-	171	$C_{18}H_{16}N_2S$	73·6	5·5	73·9	5·4
2 : 4-Dimethylphenyl-	168	$C_{19}H_{18}N_2S$	74·2	6·0	74·5	5·8
p-Ethylphenyl-	183	$C_{19}H_{18}N_2S$	74·6	6·1	74·5	5·8
p-*n*-Propylphenyl-	179	$C_{20}H_{20}N_2S$	74·9	6·2	75·0	6·2
n-Butylphenyl-	179	$C_{21}H_{22}N_2S$	75·5	6·6	75·4	6·5
o-*tert.*-Butylphenyl-	200	$C_{21}H_{22}N_2S$	75·1	6·4	75·4	6·5
p-*n*-Heptylphenyl-	176	$C_{24}H_{28}N_2S$	76·6	7·4	76·5	7·4
p-Hydroxyphenyl-	224	$C_{17}H_{14}ON_2S$	69·0	4·9	69·3	4·7
p-Methoxyphenyl-	192	$C_{18}H_{16}ON_2S$	70·0	5·1	70·1	5·1
3-Fluoro-6-methoxyphenyl-	137	$C_{18}H_{15}ON_2SF$	66·0	4·8	66·2	4·6
2 : 5-Dimethoxyphenyl-	166	$C_{19}H_{18}O_2N_2S$	67·5	5·5	67·4	5·3
p-Phenetyl-	190	$C_{19}H_{18}ON_2S$	70·7	5·4	70·8	5·5
p-*iso*Butoxyphenyl-	179	$C_{21}H_{22}ON_2S$	71·8	6·4	72·0	6·2
p-*n*-Butoxyphenyl-	185	$C_{21}H_{22}ON_2S$	72·1	6·1	72·0	6·2
p-*n*-Heptyloxyphenyl-	176	$C_{24}H_{28}ON_2S$	73·3	7·3	73·4	7·1
p-3-Phenylpropoxyphenyl-	171	$C_{26}H_{24}ON_2S$	75·4	6·0	75·7	5·8
o-Methylthiophenyl-	205	$C_{18}H_{16}N_2S_2$	66·5	5·0	66·6	4·9
o-Methylselenophenyl-	210	$C_{18}H_{16}N_2SSe$	59·0	4·1	59·1	4·3
p-Dimethylaminophenyl-	172	$C_{19}H_{19}N_3S$	70·8	6·0	71·0	5·9
4-Diphenylyl-	242	$C_{25}H_{18}N_2S$	78·0	5·1	77·9	5·0
2-Diphenylyl-	192	$C_{25}H_{18}N_2S$	77·9	5·3	77·9	5·0
4-Chloro-1-naphthyl-	189	$C_{21}H_{15}N_2SCl$	69·2	4·3	69·5	4·1

TABLE 2. (*Continued.*)

R′	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
R = 2-pyridyl.						
p-Fluorophenyl-	178°	$C_{12}H_{10}N_3SF$	58·0	4·0	58·2	4·0
p-Chlorophenyl-	208	$C_{12}H_{10}N_3SCl$	54·3	3·8	54·6	3·7
p-Bromophenyl-	224	$C_{12}H_{10}N_3SBr$	46·4	3·2	46·6	3·2
p-Tolyl-	192	$C_{13}H_{13}N_3S$	64·0	5·5	64·1	5·3
m-Tolyl-	174	$C_{13}H_{13}N_3S$	64·2	5·3	64·1	5·3
2 : 4-Dimethylphenyl-	193	$C_{14}H_{15}N_3S$	65·0	6·0	65·3	5·8
p-*n*-Butylphenyl-	156	$C_{16}H_{19}N_3S$	67·3	6·8	67·3	6·6
p-Methoxyphenyl-	208	$C_{12}H_{13}ON_3S$	60·1	5·3	60·2	5·0
p-Phenetyl-	209	$C_{14}H_{15}ON_3S$	61·3	5·5	61·5	5·4
p-*n*-Propoxyphenyl-	171	$C_{15}H_{17}ON_3S$	62·8	6·2	62·7	5·9
p-*n*-Butoxyphenyl-	149	$C_{16}H_{19}ON_3S$	63·8	6·5	63·7	6·3
p-*iso*Pentyloxyphenyl-	146	$C_{17}H_{21}ON_3S$	64·4	6·7	64·7	6·6
2-Diphenylyl-	176	$C_{18}H_{15}N_3S$	70·5	5·1	70·8	4·9
1-Naphthyl-	236	$C_{16}H_{13}N_3S$	68·6	4·5	68·8	4·6
2-Naphthyl-	242	$C_{16}H_{13}N_3S$	68·5	4·3	68·8	4·6
R = 2-thiazolyl.						
p-Fluorophenyl-	181	$C_{10}H_6N_3S_2F$	47·3	3·1	47·4	3·1
p-Chlorophenyl-	204	$C_{10}H_6N_3S_2Cl$	44·3	3·1	44·5	2·9
p-Bromophenyl-	206	$C_{10}H_6N_3S_2Br$	38·0	2·8	38·2	2·5
p-Tolyl-	201	$C_{11}H_{11}N_3S_2$	53·1	4·7	53·0	4·4
2 : 4-Dimethylphenyl-	204	$C_{12}H_{13}N_3S_2$	54·6	4·7	54·7	4·9
p-*n*-Propylphenyl-	204	$C_{12}H_{15}N_3S_2$	56·5	5·3	56·3	5·4
p-Methoxyphenyl-	212	$C_{11}H_{11}ON_3S_2$	49·6	4·1	49·8	4·1
p-Phenetyl-	203	$C_{12}H_{13}ON_3S_2$	51·3	4·5	51·6	4·6
1-Naphthyl-	235	$C_{14}H_{11}N_3S_2$	59·0	3·5	58·9	3·8
2-Naphthyl-	232	$C_{14}H_{11}N_3S_2$	58·6	3·9	58·9	3·8
Various thioureas.						
NN′-Di-(1 : 2-dihydroindan-5-yl)-	127—128	$C_{19}H_{20}NS$	74·2	6·5	74·0	6·4
NN′-Di-(4-chloro-1-naphthyl)-	202	$C_{21}H_{14}N_2SCl_2$	63·3	3·6	63·4	3·5
N-(4-Chloro-1-naphthyl)-*N*′-*p*-fluorophenyl-	199	$C_{17}H_{12}N_2SClF$	61·5	3·5	61·8	3·6
N-(4-Chloro-1-naphthyl)-*N*′-2-diphenylyl-	198	$C_{23}H_{17}N_2SCl$	70·9	4·5	71·0	4·3
N-*p*-Butoxyphenyl-*N*′-(5-hydroxy-1-naphthyl)-	181	$C_{21}H_{28}O_2N_2S$	68·6	6·2	68·8	6·0
N-(6-Methyl-2-pyridyl)-*N*′-1-naphthyl-	212	$C_{17}H_{15}N_3S$	69·8	5·0	69·6	5·1
N-(6-Methyl-2-pyridyl)-*N*′-2-naphthyl-	252	$C_{17}H_{15}N_3S$	69·5	5·3	69·6	5·1
NN′-Di-2-thiazolyl-	260	$C_7H_6N_4S_2$	34·5	2·7	34·7	2·4

p-Alkyloxyanilines were prepared in good yields (75—90%) by refluxing for 4—6 hr. an ethanol solution of *p*-formamidophenol (1 mol.) and potassium hydroxide (1 mol.) with the appropriate alkyl bromide (1 mol.), and subsequent alkaline hydrolysis of the crude *p*-alkyloxyformanilide. The following amines were thus obtained: p-iso-*Propoxyaniline*, pale yellow oil darkening rapidly on exposure to the air, b. p. 146—147°/15 mm., n_D^{18} 1·5471 (Found: C, 71·4; H, 8·5. $C_9H_{13}ON$ requires C, 71·5; H, 8·6%); *p*-*n*-propoxyaniline, n_D^{25} 1·5455; *p*-*n*-butoxyaniline, n_D^{28} 1·5398; *p*-*iso*butoxyaniline, b. p. 149—150°/15 mm.; *p*-*iso*pentyloxyaniline, n_D^{26} 1·5302; p-n-*pentyloxyaniline*, b. p. 175—176°/17 mm., n_D^{26} 1·5345 (Found: C, 73·5; H, 9·6. $C_{11}H_{17}ON$ requires C, 73·7; H, 9·5%); p-n-*heptyloxyaniline*, b. p. 202—204°/16 mm., shiny leaflets, m. p. 46—47° (from ligroin) (Found: C, 75·3; H, 10·2. $C_{13}H_{21}ON$ requires C, 75·4; H, 10·1%); p-3′-*phenylpropoxyaniline*, b. p. 234—236°/15 mm., colourless needles, m. p. 58° (from ligroin) (Found: C, 79·1; H, 7·4. $C_{15}H_{17}ON$ requires C, 79·3; H, 7·5%). *p*-Alkyloxyanilines have usually been prepared in low yields by reduction of the corresponding nitro-compounds (cf. Spiegel and Sabbath, *Ber.*, **1901**, **34**, 1938; Gutekunst and Gray, *J. Amer. Chem. Soc.*, 1922, **44**, 1744), or by alkylation of *p*-benzylideneaminophenol and subsequent hydrolysis (Philipp, *Ber.*, 1892, **25**, 3248; Höchster Farbwerke, D.R.-P. 69,006).

Characterisation of the Amines.—Condensation of the amines (1 mol.) with acetonylacetone (1·5 mol.) was effected by refluxing the mixture for 30 min., and the 1-*aryl*-2 : 5-*dimethylpyrroles* formed (Table 3) were distilled *in vacuo*; the solid products were crystallised from methanol (the yields range from 90 to 100%). Table 4 records new 2-*arylamino*-3-*chloro*-1 : 4-*naphthaquinones*, obtained by briefly refluxing an ethanol solution of the arylamine (1 mol.), 2 : 3-dichloro-1 : 4-naphthaquinone (1 mol.), and sodium acetate (1 mol.); the precipitate obtained on

TABLE 3. *N-Substituted* 2 : 5-*dimethylpyrroles.*

N-Substituent	B. p./mm.	M. p.	n	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
p-n-Propoxyphenyl-	176°/13	47°	—	$C_{15}H_{19}ON$	78·5	8·5	78·6	8·2
*p-iso*Propoxyphenyl-	177/25	—	n_D^{18} 1·5485	$C_{15}H_{19}ON$	78·3	8·1	78·6	8·2
*p-iso*Butoxyphenyl-	179/14	45	—	$C_{16}H_{21}ON$	78·8	8·9	79·0	8·6
p-n-Butoxyphenyl-	186/13	39	—	$C_{16}H_{21}ON$	79·1	8·5	79·0	8·6
*p-iso*Pentyloxyphenyl- ...	189/13	—	$n_D^{18\cdot5}$ 1·4675	$C_{17}H_{23}ON$	79·0	9·1	79·3	8·9
p-n-Pentyloxyphenyl-	189—192/13	—	n_D^{21} 1·4557	$C_{17}H_{23}ON$	79·3	9·1	79·3	8·9
p-n-Heptyloxyphenyl- ...	222/15	—	n_D^{18} 1·4355	$C_{19}H_{27}ON$	79·9	9·3	80·0	9·4
p-3-Phenylpropoxyphenyl-	260/16	68—69	—	$C_{21}H_{25}ON$	82·3	7·6	82·6	7·5
o-Ethoxyphenyl-	158—160/13	—	$n_D^{18\cdot5}$ 1·5404	$C_{14}H_{17}ON$	78·0	7·9	78·1	7·9
p-n-Propylphenyl-	164/23	—	n_D^{25} 1·5479	$C_{15}H_{19}N$	84·7	8·8	84·5	8·9
p-n-Butylphenyl-	178/25	—	n_D^{24} 1·5426	$C_{16}H_{21}N$	84·5	9·5	84·5	9·2
p-n-Heptylphenyl-	208/25	—	n_D^{25} 1·5296	$C_{19}H_{27}N$	84·9	10·2	84·7	10·0
o-Methylthiophenyl-	—	91	—	$C_{12}H_{15}NS$	71·5	6·9	71·8	6·9

TABLE 4. 2-*Substituted* 3-*chloro*-1 : 4-*naphthaquinones.*

2-Substituent	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
p-n-Propylanilino-	141°	$C_{19}H_{16}O_2NCl$	69·8	4·6	70·0	4·9
p-n-Butylanilino-	139	$C_{20}H_{18}O_2NCl$	70·3	5·1	70·6	5·3
p-n-Heptylanilino-	124	$C_{23}H_{24}O_2NCl$	72·1	6·1	72·3	6·2
p-n-Propoxyanilino-	162	$C_{19}H_{16}O_3NCl$	66·8	4·6	66·7	4·6
*p-iso*Propoxyanilino-	176	$C_{19}H_{16}O_3NCl$	66·5	4·5	66·7	4·6
p-n-Butoxyanilino-	155	$C_{20}H_{18}O_3NCl$	67·2	5·2	67·5	5·0
*p-iso*Butoxyanilino-	181	$C_{20}H_{18}NCl$	67·5	5·1	67·5	5·0
p-n-Pentyloxyanilino-	147	$C_{21}H_{20}O_3NCl$	68·0	5·6	68·2	5·4
*p-iso*Pentyloxyanilino-	145	$C_{21}H_{20}O_3NCl$	68·3	5·5	68·2	5·4
p-n-Heptyloxyanilino-	136	$C_{23}H_{24}O_3NCl$	69·6	6·1	69·4	6·0
p-3-Phenylpropoxyanilino-	170	$C_{25}H_{20}O_3NCl$	72·0	4·9	71·8	4·7
3 : 4-Dichloroanilino- [a]	246	$C_{16}H_8O_2NCl_3$	54·1	2·5	54·4	2·2
2-Methoxy-5-methylanilino-	157	$C_{18}H_{14}O_3NCl$	65·8	4·2	65·9	4·2

[a] 2 : 5-Dichloroaniline did not give a normal condensation product.

TABLE 5. 2 : 5-*Disubstituted* 3 : 6-*dichloro*-1 : 4-*benzoquinones.*

2 : 5-Substituents	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
p-n-Propylanilino-	268°	$C_{24}H_{24}O_2N_2Cl_2$	64·7	5·5	65·0	5·4
p-n-Butylanilino-	264	$C_{26}H_{28}O_2N_2Cl_2$	66·0	5·9	66·2	5·9
p-n-Heptylanilino-	212	$C_{32}H_{40}O_2N_2Cl_2$	69·0	7·1	69·1	7·2
p-n-Propoxyanilino-	254	$C_{24}H_{24}O_4N_2Cl_2$	60·3	5·2	60·6	5·0
*p-iso*Propoxyanilino-	>300	$C_{24}H_{24}O_4N_2Cl_2$	60·5	4·8	60·6	5·0
p-n-Butoxyanilino-	248	$C_{26}H_{28}O_4N_2Cl_2$	61·9	5·4	62·0	5·5
*p-iso*Butoxyanilino-	278	$C_{26}H_{28}O_4N_2Cl_2$	62·2	5·5	62·0	5·5
p-n-Pentyloxyanilino-	241	$C_{28}H_{32}O_4N_2Cl_2$	63·1	6·3	63·3	6·0
*p-iso*Pentyloxyanilino-	262	$C_{28}H_{32}O_4N_2Cl_2$	63·3	5·9	63·2	6·0
p-n-Heptyloxyanilino-	234	$C_{32}H_{40}O_4N_2Cl_2$	65·1	7·0	65·4	6·8
p-3-Phenylpropoxyanilino-	228	$C_{30}H_{32}O_4N_2Cl_2$	68·7	5·0	68·8	5·1
3 : 4-Dichloroanilino- [a]	>320	$C_{18}H_8O_2N_2Cl_6$	43·1	1·9	43·4	1·6
2-Methoxy-5-methylanilino-	263	$C_{32}H_{26}O_4N_2Cl_2$	58·8	4·3	59·0	4·4

[a] 2 : 5-Dichloroaniline did not give a normal condensation product.

cooling was crystallised from ethanol. 2 : 5-*Bisarylamino*-3 : 6-*dichloro*-1 : 4-*benzoquinones*, similarly prepared from chloranil (1 mol.) and the appropriate arylamine (2 mol.), were recrystallised from ethanol or ethanol–pyridine; they are listed in Table 5 (yields: 80 to 98%).

Preparation of Aryl iso*Thiocyanates.*—A solution of the appropriate thiocarbanilide (1 mol.) in acetic anhydride (2 mol.) was gently refluxed for 10 min., the resulting mixture slowly fractionated *in vacuo*, and the *iso*thiocyanate, obtained in 80—90% yield, was redistilled; the new aryl *iso*thiocyanates are listed in Table 6.

Preparation of Disubstituted Thioureas.—(a) *Unsymmetrical thioureas.* A solution of equimolecular amounts of the appropriate arylamine and aryl *iso*thiocyanate in a few drops of ethanol was heated at 45—50° for some minutes; in most instances, the thiourea formed solidified immediately and was recrystallised from methanol, ethanol, or ethanol–benzene. In the case of *o*-substituted arylamines or aryl *iso*thiocyanate, the thiourea was formed more slowly,

TABLE 6. *Aryl* isothiocyanates.

	B. p./mm.	n	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
p-n-Propylphenyl [a]	150°/15	$n_D^{22.5}$ 1·5942	$C_{10}H_{11}NS$	—	—	—	—
p-n-Butylphenyl	162/15	n_D^{15} 1·5880	$C_{11}H_{13}NS$	69·0	6·9	69·1	6·8
p-n-Heptylphenyl [b]	205—207/20	—	$C_{14}H_{19}NS$	72·3	8·0	72·1	8·1
p-n-Propoxyphenyl	174/15	n_D^{22} 1·6072	$C_{10}H_{11}ONS$	62·1	5·6	62·1	5·6
*p-iso*Propoxyphenyl	170/17	n_D^{19} 1·6056	$C_{10}H_{11}ONS$	62·2	5·8	62·1	5·6
p-n-Butoxyphenyl	190—191/16	n_D^{17} 1·5942	$C_{11}H_{13}ONS$	63·6	6·5	63·7	6·2
p-n-Pentyloxyphenyl	202—204/16	n_D^{17} 1·5726	$C_{12}H_{15}ONS$	65·0	7·0	65·1	6·7
*p-iso*Pentyloxyphenyl [c]	195—196/15	n_D^{25} 1·5802	$C_{12}H_{15}ONS$	65·2	6·9	65·1	6·7
p-Fluorophenyl	215	n_D^{25} 1·6116	C_7H_4NSF	54·8	2·6	54·9	2·6
2-Diphenylyl-	312/32	n_D^{26} 1·6162	$C_{13}H_9NS$	73·9	4·5	73·9	4·2
2 : 3-Dimethylphenyl [d]	146/13	n_D^{19} 1·6119	C_9H_9NS	—	—	—	—
2 : 4-Dimethylphenyl [e]	144—145/16	n_D^{25} 1·6102	C_9H_9NS	—	—	—	—

[a] Francksen (*loc. cit.*) gave b. p. 263°. [b] Solidified at room temperature to a fat-like mass. [c] Crystallised as long flat prisms, m. p. 42°, from ligroin. [d] Prepared by a different method by Dyson, George, and Hunter (*J.*, 1927, 440), who gave b. p. 262—263°/760 mm. [e] Prepared by Werner (*J.*, 1891, **59**, 405).

and with *o*-trifluoromethylaniline only the symmetrical thiourea corresponding to the aryl *iso*thiocyanate was isolated.

(b) *Symmetrical thioureas.* A mixture of the arylamine (2 mol.), sulphur (0·5 mol.), carbon disulphide (2 mol.), and ethanol was gently refluxed for 24 hr., the mixture obtained filtered, and the filtrate concentrated. The thiourea formed was recrystallised from methanol, ethanol, or ethanol–benzene; the yields range from 90 to 100%.

All these thioureas undergo thermal decomposition on prolonged heating below their m. p.s; the m. p.s therefore depend to a great extent on the speed of heating. This accounts for the wide discrepancies recorded at times in the literature. In the present work m. p.s were taken with a Maquenne block, and represent the point of instantaneous liquefaction.

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*Thiophen Derivatives of Biological Interest. Part X.** *5-Substituted 2-Thenaldehydes and Derivatives.*

By NG. PH. BUU-HOÏ, DENISE LAVIT, and NG. D. XUONG.

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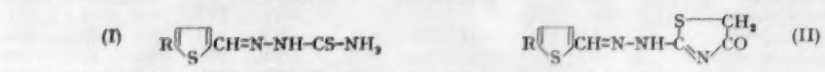
A number of new 2-thenaldehydes bearing alkyl, arylalkyl, and *cyclo*hexylalkyl substituents at position 5 have been synthesised, and their thiosemicarbazones and 4-oxo-Δ^2-thiazolin-2-ylhydrazones prepared for testing for tuberculostatic and tumour-growth inhibiting activity.

THIOSEMICARBAZONES of many 5-substituted 2-thenaldehydes display high tuberculostatic activity *in vitro* (Welsch, Buu-Hoï, Dechamps, Hoán, Le Bihan, and Binon, *Compt. rend.*, 1951, **232**, 1608). This activity decreases with the length of the chain in position 5, *e.g.*, against *Mycobacterium tuberculosis, var. hominis* (strain H37 Rv), as 5-*n*-propyl-2-thenaldehyde thiosemicarbazone (Buu-Hoï, Xuong, Royer, and Lavit, *J.*, 1953, 547) is active at the concentration $1 : 10^6$—10^7, and the undecyl, dodecyl, and tetradecyl analogues at $1 : 10^4$; also 5-*n*-tetradecyl-2-thenaldehyde thiosemicarbazone shows a slight inhibitory activity towards the growth of grafted sarcoma 180 in mice at a daily dose of 200 mg./kg. (personal communication from Dr. Chester Stock, Sloan-Kettering Institute, New York). A number of new 5-substituted 2-thenaldehydes, their thiosemicarbazones (I), and their 4-oxo-Δ^2-thiazolin-2-ylhydrazones (II) have now been prepared for further biological experiments. The substituents at position 5 include straight and branched alkyl, arylalkyl, and *cyclo*hexylalkyl groups. The aldehydes were synthesised by the

* Part IX, Sy, Buu-Hoï, and Xuong, *J.*, 1955, 21.

N-methylformanilide reaction (King and Nord, *J. Org. Chem.*, 1948, **13**, 635; Buu-Hoï *et al.*, *J.*, 1952, 4590; 1953, 547) on the appropriate 5-substituted thiophens, prepared by reduction of 2-acylthiophens. Condensation of the new thienaldehydes with *iso*nicotinoylhydrazine gave the hydrazones, listed on p. 1583. The 4-oxo-Δ^2-thiazolin-2-ylhydrazones



(I) (II)

of the aldehydes described were prepared from the corresponding thiosemicarbazones and chloroacetic acid (Chabrier *et al.*, *Bull. Soc. chim. France*, 1947, **14**, 797; 1950, **17**, 48; Buu-Hoï *et al.*, *loc. cit.*).

Experimental

Friedel–Crafts Acylations of Thiophen.—The reactions between thiophen and acid chlorides were catalysed with stannic chloride in carbon disulphide solution, in the usual way (cf. Sy, Buu-Hoï, and Xuong, *J.*, 1954, 1975); some of the ketones thus prepared were insufficiently characterised or were unknown, *viz.*: 2-Hexanoylthiophen, b. p. 159°/13 mm., n_D^{24} 1·5285 (Schleicher, *Ber.*, 1886, **19**, 660, gave b. p. 304°/760 mm.) [*semicarbazone*, needles, m. p. 117°, from ethanol (Found: N, 16·3. $C_{12}H_{19}ON_3S$ requires N, 16·6%)]. 2-*n*-Decanoylthiophen, b. p. 205°/22 mm., n_D^{27} 1·5170 (cf. Cagniant and Deluzarche, *Compt. rend.*, 1947, **225**, 455) [semicarbazone, m. p. 114° (Hartough and Kosak, *J. Amer. Chem. Soc.*, 1947, **69**, 3098, gave m. p. 110—110·5°)]. 2-*Hexahydrobenzoylthiophen*, b. p. 162°/13 mm., prisms, m. p. 44°, from ligroin (Found: C, 68·0; H, 7·4. $C_{11}H_{14}OS$ requires C, 68·0; H, 7·2%) [*semicarbazone*, prisms, m. p. 152°, from ethanol (Found: N, 16·9. $C_{12}H_{17}ON_3S$ requires N, 16·7%)]. 2-β-cyclo*Hexylpropionylthiophen*, b. p. 188°/13 mm., n_D^{18} 1·5542 (Found: C, 70·0; H, 8·3. $C_{13}H_{18}OS$ requires C, 70·3; H, 8·1%). 2-4′-cyclo*Hexylhexanoylthiophen*, b. p. 217°/14 mm., n_D^{24} 1·5428 (Found: C, 72·4; H, 9·2. $C_{16}H_{24}OS$ requires C, 72·7; H, 9·1%) [*semicarbazone*, prisms, m. p. 149°, from methanol (Found: N, 13·2. $C_{17}H_{27}ON_3S$ requires N, 13·1%)]. 2-ω-cyclo*Pentyltridecanoylthiophen*, b. p. 260—263°/13 mm., n_D^{26} 1·5205 (Found: C, 75·6; H, 10·3. $C_{22}H_{36}OS$ requires C, 75·9; H, 10·3%).

Reduction of 2-Acylthiophens.—This was performed by Huang-Minlon's method in diethylene glycol; yields were excellent (80—98%), except with the long-chain ketones.

Formylation of 5-Substituted Thiophens.—This was effected equally well with *N*-methylformanilide or dimethylformamide, provided that with the latter agent the heating was prolonged (10—12 hr.).

Products.—See Tables.

2-Alkyl-, 2-arylalkyl-, and 2-cycloalkyl-thiophens.

Substituent [a]	B. p./mm.	n_D (temp.)	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
n-Butyl- [b]	182°	1·5070 (24)	$C_8H_{12}S$	—	—	—	—
*iso*Pentyl- [c]	196—198	1·5040 (24)	$C_9H_{14}S$	—	—	—	—
n-Pentyl-	204	1·5055 (20)	$C_9H_{14}S$	70·0	9·2	70·1	9·1
n-Hexyl- [d]	114/14	1·5026 (24)	$C_{10}H_{16}S$	—	—	—	—
n-Heptyl-	127/18	1·4998 (24)	$C_{11}H_{18}S$	72·3	9·9	72·5	9·9
n-Octyl- [e]	139/15	1·4970 (23)	$C_{12}H_{20}S$	73·5	10·1	73·5	10·2
n-Decyl-	170/16	1·4932 (27)	$C_{14}H_{24}S$	74·8	10·8	75·0	10·7
4′-*tert.*-Butylbenzyl-	177/14	1·5635 (26)	$C_{15}H_{18}S$	78·2	7·8	78·3	7·8
*cyclo*Hexylmethyl-	129/18	1·5350 (24)	$C_{11}H_{16}S$	73·5	8·8	73·3	8·9
3′-*cyclo*Hexyl-*n*-propyl-	157/13	1·5272 (21)	$C_{12}H_{20}S$	75·1	9·8	75·0	9·6
4′-*cyclo*Hexyl-*n*-hexyl-	185—187/15	1·5220 (21)	$C_{16}H_{26}S$	76·8	10·6	76·8	10·4
ω-*cyclo*Pentyl-*n*-tridecyl-	242—248/20	1·5045 (24)	$C_{22}H_{36}S$	78·8	11·5	79·0	11·4
2-*n*-Hexyl-5-methyl-	116/14	1·5010 (24)	$C_{11}H_{18}S$	72·3	9·9	72·5	9·9
2-*n*-Heptyl-5-methyl-	129/15	1·4982 (24)	$C_{12}H_{20}S$	73·5	10·5	73·5	10·2
2-*cyclo*Hexylmethyl-5-methyl-	141/22	1·5330 (20)	$C_{12}H_{18}S$	74·0	9·3	74·2	9·3
β-Phenethyl- [a]	152/15	1·5854 (24)	$C_{12}H_{12}S$	—	—	—	—

[a] At position 2 unless otherwise stated. [b] Meyer and Kreis (*Ber.*, 1884, **17**, 1559) gave b. p. 181—182°. [c] Steinkopf and Schubart (*Annalen*, 1920, **424**, 1) gave b. p. 74—75°/11 mm. [d] Campaigne and Diedrich (*J. Amer. Chem. Soc.*, 1948, **70**, 391) gave b. p. 79—82°/1 mm., n_D^{20} 1·4970. [e] von Schweinitz (*Ber.*, 1886, **19**, 644) gave b. p. 257—259°, and Campaigne and Diedrich (*loc. cit.*) gave b. p. 106—108°/1 mm., n_D^{20} 1·4824. [f] Buu-Hoï, Hoán, and Jacquignon (*J.*, 1951, 1381) gave b. p. 159—160°/13 mm.; this substance is a liquid, and the m. p. cited was a clerical error.

5-Substituted 2-thenaldehydes.

5-Substituent	B. p./mm.	*n* (temp.)	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
n-Butyl-	145°/18	1·5517 (26)	$C_9H_{12}OS$	64·1	7·3	64·3	7·1
*iso*Pentyl-	152—154/18	1·5460 (25)	$C_{10}H_{14}OS$	65·8	7·6	65·9	7·7
n-Pentyl-	150/14	1·5480 (19)	$C_{10}H_{14}OS$	65·8	7·9	65·9	7·7
n-Hexyl-	160/13	1·5415 (23)	$C_{11}H_{16}OS$	67·1	8·1	67·3	8·2
n-Heptyl-	173/13	1·5338 (26)	$C_{12}H_{18}OS$	68·5	8·5	68·6	8·6
n-Octyl-	190/14	1·5310 (25)	$C_{13}H_{20}OS$	69·3	9·1	69·6	8·9
n-Decyl-	210—212/14	1·5250 (24)	$C_{15}H_{24}OS$	71·3	9·6	71·4	9·5
Phenethyl-	208/14	1·6165 (24)	$C_{12}H_{12}OS$	72·2	5·5	72·2	5·6
4′-*tert.*-Butylbenzyl-	218—220/13	1·5910 (24)	$C_{16}H_{18}OS$	74·3	6·9	74·4	7·0
*cyclo*Hexylmethyl-	180/13	1·5708 (23)	$C_{12}H_{16}OS$	69·0	7·9	69·2	7·7
3′-*cyclo*Hexyl-*n*-propyl-	215/18	1·5550 (24)	$C_{14}H_{20}OS$	71·2	8·8	71·2	8·5
4′-*cyclo*Hexyl-*n*-hexyl-	236/17	1·5470 (23)	$C_{17}H_{26}OS$	73·3	9·3	73·4	9·4
ω-*cyclo*Pentyl-*n*-tridecyl- [a]	270—275/15	1·5219 (22)	$C_{23}H_{38}OS$	76·0	10·3	76·2	10·5

[a] The 2 : 4-*dinitrophenylhydrazone* formed red needles, m. p. 155°, from acetic acid (Found : N, 10·6. $C_{29}H_{32}O_4N_4S$ requires N, 10·3%); the p-*chlorobenzoylhydrazone*, prisms, m. p. 126°, from ethanol (Found : C, 69·6; H, 8·5. $C_{30}H_{43}ON_2SCl$ requires C, 69·9; H, 8·3%); the *salicyloylhydrazone*, prisms, m. p. 151°, from ethanol (Found : N, 5·7. $C_{30}H_{44}O_3N_2S$ requires N, 5·6%); and the 5-*chlorosalicyloylhydrazone*, prisms, m. p. 170°, from ethanol (Found : C, 67·5; H, 8·3. $C_{30}H_{43}O_3N_2SCl$ requires C, 67·8; H, 8·1%).

5-Substituted 2-thenaldehyde thiosemicarbazones.[a]

Substituent	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
n-Butyl-	105°	$C_{10}H_{15}N_3S_2$	56·2	6·5	56·0	6·2
*iso*Amyl-	121	$C_{11}H_{17}N_3S_2$	51·5	6·9	51·8	6·7
n-Amyl-	106	$C_{11}H_{17}N_3S_2$	51·8	6·9	51·8	6·7
n-Hexyl-	99	$C_{12}H_{19}N_3S_2$	53·2	7·0	53·5	7·1
n-Heptyl-	102	$C_{13}H_{21}N_3S_2$	55·0	7·7	55·1	7·4
n-Octyl-	94	$C_{14}H_{23}N_3S_2$	56·8	7·7	56·6	7·7
n-Decyl-	92	$C_{16}H_{27}N_3S_2$	59·3	8·5	59·1	8·3
Phenethyl-	141	$C_{14}H_{15}N_3S_2$	58·0	5·4	58·1	5·2
4′-*tert.*-Butylbenzyl-	170 (dec.)	$C_{17}H_{21}N_3S_2$	61·3	6·5	61·6	6·3
*cyclo*Hexylmethyl-	147	$C_{13}H_{19}N_3S_2$	55·4	6·8	55·5	6·8
3′-*cyclo*Hexylpropyl-	150	$C_{15}H_{23}N_3S_2$	58·5	7·2	58·2	7·4
4′-*cyclo*Hexyl-*n*-hexyl-	91	$C_{18}H_{29}N_3S_2$	61·6	8·6	61·5	8·3
ω-*cyclo*Pentyl-*n*-tridecyl-	82	$C_{24}H_{41}N_3S_2$	66·5	9·7	66·2	9·4

[a] Recrystallised from ethanol.

5-Substituted 2-thenaldehyde derivatives.

	4-Oxo-Δ²-thiazolin-2-ylhydrazones.[a]						*iso*Nicotinoylhydrazones[b]			
Substituent	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H	M. p.	Formula	Found (%) N	Reqd. (%) N
n-Butyl-	195° (dec.)	$C_{12}H_{15}ON_3S_2$	51·0	5·2	51·2	5·3	148°	$C_{15}H_{17}ON_3S$	14·5	14·6
*iso*Pentyl-	198	$C_{13}H_{17}ON_3S_2$	52·6	6·0	52·9	5·8	162	$C_{16}H_{19}ON_3S$	14·0	14·0
n-Pentyl-	194	$C_{13}H_{17}ON_3S_2$	52·6	5·8	52·9	5·8	130	$C_{16}H_{19}ON_3S$	14·2	14·0
n-Hexyl-	178	$C_{14}H_{19}ON_3S_2$	54·3	6·1	54·4	6·2	121	$C_{17}H_{21}ON_3S$	13·0	13·3
n-Heptyl-	180	$C_{15}H_{21}ON_3S_2$	55·9	6·5	55·7	6·5	122	$C_{18}H_{23}ON_3S$	12·6	12·8
n-Octyl-	168	$C_{16}H_{23}ON_3S_2$	56·8	7·0	57·0	6·8	122	$C_{19}H_{25}ON_3S$	12·1	12·2
n-Decyl-	157	$C_{18}H_{27}ON_3S_2$	59·1	7·3	59·2	7·4	124	$C_{21}H_{29}ON_3S$	11·1	11·3
Phenethyl-	217	$C_{16}H_{15}ON_3S_2$	58·1	4·9	58·4	4·6	180	$C_{19}H_{17}ON_3S$	12·2	12·5
4′-*tert.*-Butylbenzyl-	238 (dec.)	$C_{19}H_{21}ON_3S_2$	61·3	5·8	61·5	5·7	183	$C_{23}H_{23}ON_3S$	11·0	11·1
*cyclo*Hexylmethyl-	240 (dec.)	$C_{15}H_{19}ON_3S_2$	56·3	5·8	56·1	5·9	187	$C_{18}H_{21}ON_3S$	12·6	12·8
3′-*cyclo*Hexylpropyl-	218 (dec.)	$C_{17}H_{23}ON_3S_2$	58·6	6·9	58·5	6·6	144	$C_{20}H_{25}ON_3S$	12·0	11·8
4′-*cyclo*Hexyl-*n*-hexyl-	170	$C_{20}H_{29}ON_3S_2$	61·1	7·6	61·4	7·4	116	$C_{29}H_{43}ON_3S$	9·0	8·7
ω-*cyclo*Pentyl-*n*-tridecyl-	152	$C_{26}H_{41}ON_3S_2$	66·0	8·4	65·7	8·6				

[a] Recrystallised from ethanol or acetic acid. [b] Recrystallised from ethanol.

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An X-Ray Examination of Long-chain Alkyl Dihydrogen Phosphates and Dialkyl Hydrogen Phosphates and Their Sodium Salts.

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A series of long-chain alkyl dihydrogen phosphates and one of dialkyl hydrogen phosphates (even members, C_{12}—C_{18}), and their sodium salts, have been prepared, and their *X*-ray spacings determined. The structures of these compounds are discussed.

In view of their relation to the phosphatides, we have examined a series of long-chain alkyl phosphates, even members C_{12}—C_{18}, of which only the hexadecyl have previously been studied. Biehringer (*Ber.*, 1905, **38**, 3974) prepared monohexadecyl dihydrogen phosphate by the action of phosphoric oxide on hexadecanol, a reaction shown later by Cherbuliez and Weniger (*Helv. Chim. Acta*, 1946, **29**, 2006) to yield both mono- and di-esters. Plimmer and Burch (*J.*, 1929, 297) prepared monohexadecyl dihydrogen and an impure dihexadecyl hydrogen phosphate, by the action of phosphoryl chloride on hexadecanol. Christiansen (*J. Biol. Chem.*, 1940, **135**, 399) criticised this work, and pointed out that Plimmer and Burch's method of isolation of the monoester depends on the solubility of the barium salt, which is, in fact, insoluble. As will be seen later, however, Christiansen's method of extraction is not free from criticism.

Investigation of the above methods of preparation shows that both give rise to mixtures of mono- and di-esters, which are difficult to separate. To a certain extent it is possible to direct the phosphoryl chloride reaction by the addition of quinoline or pyridine, which favour mono- and di-ester formation respectively; nevertheless, the products are invariably mixtures.

We have therefore used diphenyl phosphorochloridate and phenyl phosphorodichloridate, and have removed the phenyl groups by catalytic hydrogenolysis (cf. Brigl and Müller, *Ber.*, 1939, **72**, 2121; Van der Neut, Uhlenbroek, and Verkade, *Rec. Trav. chim.*, 1953, **72**, 395). As the latter authors showed, it is important to use an alkali-free catalyst in order to avoid the formation of acid sodium salts of the type, $RO{\cdot}PO(OH)_2$,$RO{\cdot}PO(OH){\cdot}ONa$. The diphenyl alkyl phosphates are low-melting solids or oils which can be purified by distillation *in vacuo*. When kept for some months they develop an odour of phenol, but they are substantially unchanged after several days' refluxing in 90% acetic acid and the only practicable way of removing the phenyl groups is catalytic hydrogenolysis.

The alkyl dihydrogen phosphates are similar to the fatty acids in solubility and in crystalline appearance, and they melt roughly 10° higher than the fatty acid of the same carbon content. They are dibasic acids, but the completely neutralised sodium salts are easily hydrolysed, and could not be obtained homogeneous enough for *X*-ray examination. Sodium hydrogen salts can be prepared pure, but these also tend to pass into quarter sodium salts.

This unusual type of salt was first described by Wagner-Jauregg and Wildermuth (*Ber.*, 1944, **77**, 481), who crystallised neutral disodium hexadecyl phosphate from acetic acid, and obtained a salt with a Na : P ratio of 1 : 2. Wagner-Jauregg, Lennartz, and Kothay (*Ber.*, 1941, **74**, 1513) had previously prepared quarter sodium salts of cholesteryl dihydrogen phosphate. Rose (*J. Amer. Chem. Soc.*, 1947, **69**, 1384) and Hunter, Roberts, and Kester (*ibid.*, 1948, **70**, 3224) obtained quarter quinoline salts of 1 : 3-phosphatidic acids, and Friedman and Seligman (*ibid.*, 1951, **73**, 5292) showed by infrared examination that the quarter sodium salt of β-naphthyl dihydrogen phosphate was an individual compound and not a mixture of sodium naphthyl hydrogen phosphate and naphthyl dihydrogen phosphate. Van der Neut *et al.* (*loc. cit.*) have characterised quarter sodium salts of the fatty acid esters of ethylene glycol dihydrogen phosphates, and converted them into the sodium-free phosphates by treatment with an ion-exchange resin (Amberlite IR-100H).

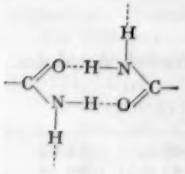
The quarter salts can be prepared by quarter-titrating the alkyl dihydrogen phosphates, by crystallising the sodium hydrogen alkyl phosphates from 90% acetic acid, or by adding a solution of alkyl dihydrogen phosphate to 10% aqueous sodium chloride. The last method is of interest in connection with the work of Christiansen (*loc. cit.*) who, in his preparation of hexadecyl dihydrogen phosphate, added a sodium chloride solution to the latter; this would certainly contaminate his product with the quarter salt. Quarter salts are not readily freed from cations by mineral acids and, in agreement with van der Neut *et al.* (*loc. cit.*), we found that this is best achieved by the use of an ion-exchange resin.

In view of the anomaly in Plimmer and Burch's paper, pointed out by Christiansen (see above), we examined the barium salts, and found that those of the higher alkyl dihydrogen phosphates (C_{12}—C_{18}) are insoluble in water (on the other hand, barium salts of lower members, at least up to C_6, are soluble in cold water, but are precipitated on boiling).

Dialkyl hydrogen phosphates are similar in appearance, and close in m. p., to the monoalkyl esters, from which they are readily distinguished, however, by exhibiting spherulite formations on solidication. They are monobasic, and form only one sodium salt, which is reconverted into the acid by crystallisation from acetic acid. We found no evidence for the existence of an acid salt similar to the quarter salt of the monoalkyl compounds.

X-Ray Investigation.—This was carried out as described by Clarkson and Malkin (*J.*, 1934, 666), Cu-K_α radiation, $\lambda = 1{\cdot}54$ Å, being used.

The results are of the expected type, and there is no indication that the presence of the large phosphate group causes any significant change in structure from the monoclinic and orthorhombic forms (tilted and vertical chains, respectively) found for fatty acids and hydrocarbons. In some cases the chains are inclined to the reflecting planes at a smaller angle than is usually found (40—45° compared with an average of about 60° for tilted forms of other long-chain compounds), and this may result merely from the larger size of the phosphate group, or it may be due to the possibility of lateral hydrogen bonding. It is of interest that long-chain fatty acid amides, which are capable of this type of bonding (see inset), are also tilted at the same low angle (44°; unpublished work).



Alkyl dihydrogen phosphates. These exist in two forms, termed A and B, in accordance with the terminology of Piper, Malkin, and Austin (*J.*, 1926, 2310). The B-form, which is the stable form, is obtained from solvents, whilst the A-form, which slowly reverts to the B-form at room temperature, is obtained when the melt solidifies.

The long spacings of both forms are linear when plotted against carbon content, and the intercepts at C = 0, which are a measure of the size of the end groups, are 8·3 (A-form) and 7·8 Å (B-form). The results (Table 1) agree with a bimolecular structure $-O{\cdot}PO(OH)_2$ $(HO)_2PO{\cdot}O-$ with the long chains tilted across the reflecting planes at angles of 41° (A-form) and 37° (B-form). No difference in m. p. was found for the two forms.

TABLE 1. *Long and short spacings for alkyl dihydrogen phosphates.*

	A-form					B-form			
	Long spacing	Short spacings				Long spacing	Short spacings		
C_{12}	29·0	4·60 w	4·13 s	3·78 s	3·54 w	26·5	4·5 s	4·18 w	3·79 s
C_{14}	32·6	4·64 w	4·14 s	3·79 s	3·53 w	29·5	4·5 s	4·19 w	3·82 s
C_{16}	35·8	4·61 w	4·12 s	3·86 s	3·53 w	32·6	4·52 s	4·14 w	3·76 s
C_{18}	39·3	4·63 w	4·16 s	3·86 s	3·54 w	35·8	4·5 s	4·16 w	3·77 s

s = strong, w = weak, m = moderate, v = very.

Sodium alkyl hydrogen phosphates. The long spacings, plotted against carbon content, are linear, and give an intercept at C = 0 of 9·5 Å. The results (Table 2) agree with a bimolecular structure $-O{\cdot}PO(OH)(ONa)$ $(NaO)(HO)PO{\cdot}O-$ with the hydrocarbon chains tilted at an angle of 40° to the reflecting planes.

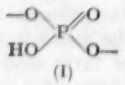
Quarter sodium salts of alkyl dihydrogen phosphates. The long spacings are linear, with an intercept C = 0 of 9·5 Å. The results (Table 2) agree with a bimolecular structure

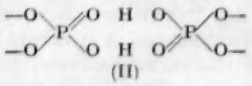
–O·PO<OH / ONa HO> PO·O– with the hydrocarbon chains tilted at an angle of 56°. The short spacings are quite different from those of either the sodium alkyl hydrogen phosphates or the alkyl dihydrogen phosphates.

TABLE 2. *X-Ray spacings for sodium salts of alkyl dihydrogen phosphates.*

	RO·PO·(OH)ONa					(RO·PO·(OH)$_2$ (HO)(NaO)PO·OR)				
	Long spacing	Short spacings				Long spacing	Short spacings			
C_{12}	28·9	5·39 w	4·66 w	4·48 m	3·76 s 3·57 vw	35·2	4·77 w	4·23 s	4·03 vw	3·75 vw 3·57 m
C_{14}	32·6	5·39 w	4·69 w	4·46 m	3·76 s 3·56 vw	39·5	4·81 w	4·19 s	4·07 vw	3·68 vw 3·58 m
C_{16}	36·1	5·34 w	4·59 w	4·44 m	3·8 s 3·62 vw	43·8	4·74 w	4·19 s	4·05 vw	3·81 vw 3·61 m
C_{18}	40·1	5·46 w	4·74 w	4·43 m	3·86 s 3·47 vw	48·2	4·73 w	4·17 s	4·00 vw	3·83 vw 3·61 m

Dialkyl hydrogen phosphates. The long spacings (Table 3) are linear and correspond to molecules tilted at an angle of 45°. The intercept at C = 0 is ≈4 Å, or slightly under a half of that found for the monoalkyl phosphates. This suggests a unimolecular structure (I) rather than the bimolecular structure (II), since the double phosphate end groups, which include hydrogen bonds, could not be accommodated in a length of 4 Å.


(I)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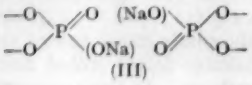

(III)

No evidence of polymorphism was observed.

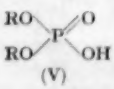
Sodium dialkyl phosphates. The *X*-ray data indicate that these crystallise in double molecules lying vertically across the reflecting planes (*i.e.*, increase in long spacing per carbon atom 1·29 Å, intercept 9 Å) (cf. III).

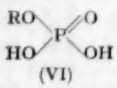
TABLE 3. *X-Ray spacings for dialkyl hydrogen phosphates and sodium dialkyl phosphates.*

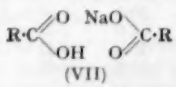
	Long spacing	Short spacings					
		(RO)$_2$PO·OH					
C_{12}	26·3	5·3 vw	4·90 vw	4·5 vs	3·85 s	3·61 m	3·4 vw
C_{14}	30·0	5·27 vw	4·87 vw	4·49 vs	3·80 s	3·61 m	3·4 vw
C_{16}	33·8	5·34 vw	4·89 vw	4·54 vs	3·80 s	3·60 m	3·4 vw
C_{18}	37·4	5·30 vw	4·88 vw	4·51 vs	3·87 s	3·61 m	3·4 vw
		(RO)$_2$PO·ONa					
C_{12}	40·3	6·07 m	5·33 vw	4·86 w	4·49 w	4·12 vs	3·73 vw
C_{14}	45·3	6·10 m	5·32 vw	4·80 w	4·51 w	4·16 vs	3·73 w
C_{16}	50·7	6·16 m	5·35 vw	4·81 w	4·47 w	4·14 vs	3·73 w
C_{18}	55·8	6·19 m	5·39 vw	4·82 w	4·51 w	4·11 vs	3·72 w

As mentioned earlier, the dialkyl phosphates do not form acid salts. This, at first sight, is surprising, particularly in view of the formal resemblance to fatty acids (IV and V) which form unusually stable acid salts (cf. Piper, *J.*, 1929, 231; Malkin, *Ber.*, 1930, **63**, 1807).

(IV)


(V)


(VI)


(VII)

It is not easy to explain why (IV) and (VI) should form acid salts of the type (VII), whilst (V) does not. A clue to this anomaly is perhaps to be found from the *X*-ray results. Both fatty acids and their salts, and alkyl dihydrogen phosphates and their monosodium salts, which combine respectively to form acid salts, have the same type of bimolecular structure. On the other hand, dialkyl phosphates and their salts have single and double molecular structures respectively, which presumably make their combination to form acid salts less probable.

Experimental

Hexadecyl Diphenyl Phosphate.—Diphenyl phosphorochloridate (8·0 g., 0·03 mole) was added slowly with shaking to a solution of hexadecan-1-ol (4·8 g., 0·02 mole) in dry pyridine (10 ml.). The flask was stoppered and set aside for 48 hr.; then the contents were poured into ice-cold N-hydrochloric acid (200 ml.). The heavy oil which separated was extracted with ether, and the ethereal layer was washed with N-hydrochloric acid (3 times), 5% sodium hydrogen carbonate (5 times), and water (5 times). After being dried (Na_2SO_4), the ether was removed, and the residue was distilled to give *hexadecyl diphenyl phosphate* (8·1 g., 85%), b. p. 190—195°/10^{-3} mm., m. p. 20—21° (Found: C, 71·1; H, 8·9; P, 6·8. $C_{28}H_{43}O_4P$ requires C, 70·9; H, 9·1; P, 6·6%).

The following were prepared similarly:

Octadecyl diphenyl phosphate (80% yield), b. p. 215—220°/10^{-3} mm., m. p. 31—32° (Found: C, 72·1; H, 9·2; P, 6·5. $C_{30}H_{47}O_4P$ requires C, 71·7; H, 9·4; P, 6·2%).

Diphenyl tetradecyl phosphate (88%), b. p. 190—5°/3×10^{-3} mm., m. p. 11—12° (Found: C, 69·7; H, 8·7; P, 7·2. $C_{26}H_{39}O_4P$ requires C, 70·0; H, 8·8; P, 7·0%).

Dodecyl diphenyl phosphate (82%), b. p. 210—215°/10^{-1} mm. m. p. −4° to −3° (Found: C, 68·8; H, 8·3; P, 7·1. $C_{24}H_{35}O_4P$ requires C, 68·9; H, 8·4; P, 7·4%).

Hexadecyl Dihydrogen Phosphate.—A suspension of platinic oxide (Adams) (0·8 g.) in glacial acetic acid (20 ml.) was shaken in hydrogen until absorption ceased (160 ml.; theor., 146 ml.). The catalyst was then well washed with 2N-hydrochloric acid, water, and finally glacial acetic acid, by decantation. Hexadecyl diphenyl phosphate (8 g.) in glacial acetic acid (100 ml.) was added to the catalyst, and the solution was shaken in hydrogen until absorption ceased (5 hr.; uptake 2990 ml.; theor., 3040 ml.). The catalyst was filtered off and washed with chloroform, and the solvents were removed from the filtrate in *vacuo*. The residue, crystallised from light petroleum (b. p. 40—60°), yielded 4·8 g. (90%) of white plates, m. p. 75—76° (Found: C, 59·8; H, 10·9; P, 9·8. Calc. for $C_{16}H_{35}O_4P$: C, 59·7; H, 10·9; P, 9·6%).

Equivalent weights were determined by titration in alcohol with aqueous 0·1N-sodium hydroxide, with bromocresol-purple and phenolphthalein for the first and the second end-point respectively (Found: 326, 165. Theor., 322; 161).

The following were prepared in the same manner:

Octadecyl dihydrogen phosphate (90%), m. p. 83° (Found: C, 61·2; H, 10·8; P, 9·2%; equiv., 353, 174. $C_{18}H_{39}O_4P$ requires C, 61·7; H, 11·2; P, 9·0%; equiv., 350, 175).

Tetradecyl dihydrogen phosphate (81%), m. p. 69° (Found: C, 57·2; H, 10·5; P, 10·8%; equiv., 290, 196. $C_{14}H_{31}O_4P$ requires C, 57·2; H, 10·6; P, 10·6%; equiv., 294, 197).

Dodecyl dihydrogen phosphate (75%), m. p. 59·5° (Found: C, 54·2; H, 10·0; P, 12·1%; equiv., 270, 132. $C_{12}H_{27}O_4P$ requires C, 54·2; H, 10·2; P, 11·7%; equiv., 266, 133).

Sodium Hexadecyl Hydrogen Phosphate.—To a warm solution of hexadecyl dihydrogen phosphate (320 mg., 0·001 mole) in neutral ethanol (15 ml.) was added 0·1N-sodium hydroxide (11 ml.). On cooling, the sodium *salt* separated (320 mg.) as colourless long, thin prisms [Found: C, 55·9; H, 10·0; P, 9·5%; equiv. (phenolphthalein), 345. $C_{16}H_{34}O_4PNa$ requires C, 55·8; H, 9·9; P, 9·0%; equiv., 344]. The following were prepared similarly:

Sodium octadecyl hydrogen phosphate (95%) (Found: C, 58·1; H, 10·2; P, 8·7%; equiv., 375. $C_{18}H_{38}O_4PNa$ requires C, 58·1; H, 10·2; P, 8·4%; equiv., 372).

Sodium tetradecyl hydrogen phosphate (86%) (Found: C, 53·6; H, 9·4; P, 9·7%; equiv., 318. $C_{14}H_{30}O_4PNa$ requires C, 53·2; H, 9·5; P, 9·8%; equiv., 316).

Sodium dodecyl hydrogen phosphate (75%) (Found: C, 49·6; H, 9·2; P, 10·6%; equiv., 280. $C_{12}H_{26}O_4PNa$ requires C, 50·1; H, 9·0; P, 10·8%; equiv., 288).

Quarter Sodium Salt of Hexadecyl Dihydrogen Phosphate.—Method 1. To hexadecyl phosphate (0·32 g., 0·001 mole) in warm ethanol (5 ml.) 0·1N-sodium hydroxide (5 ml., 0·0005 mole) was added. On cooling, the quarter sodium salt (0·3 g., 90%) separated as colourless flat prisms (Found: C, 58·0; H, 10·4; P, 9·2%; equiv., 218. $C_{32}H_{69}O_8P_2Na$ requires C, 57·7; H, 10·5; P, 9·8%; equiv., 222).

Method 2. Sodium hexadecyl hydrogen phosphate (0·17 g.) was crystallised twice from aqueous acetic acid (3 ml., 90% acid), yielding 0·12 g. (74%) of the quarter sodium salt (Found: equiv., 219).

Method 3. Hexadecyl dihydrogen phosphate (0·32 g.) was dissolved in ethanol (20 ml.) and the solution was poured into 10% aqueous sodium chloride (50 ml.). The quarter salt separated, and was filtered off and washed with water. Crystallisation from glacial acetic acid afforded 0·25 g. of product of equiv. 225.

X-Ray powder photographs of salts made by all three methods were identical.

The following were made by method 2.

Quarter sodium salt of octadecyl dihydrogen phosphate (94%) (Found : C, 60·2; H, 10·5; P, 8·6%; equiv., 244. $C_{36}H_{77}O_8P_2Na$ requires C, 59·8; H, 10·8; P, 8·6%; equiv., 241.

Quarter sodium salt of tetradecyl dihydrogen phosphate (82%) (Found : C, 55·1; H, 9·9; P, 10·1%; equiv., 203. $C_{28}H_{61}O_8P_2Na$ requires C, 55·1; H, 10·1; P, 10·1%; equiv., 204).

Quarter sodium salt of dodecyl dihydrogen phosphate (72%) (Found : C, 51·7; H, 9·5; P, 11·3%; equiv., 194. $C_{24}H_{53}O_8P_2Na$ requires C, 52·0; H, 9·7; P, 11·2%; equiv., 198).

Conversion of Quarter Sodium Salt of Hexadecyl Dihydrogen Phosphate into Hexadecyl Dihydrogen Phosphate. A solution of the quarter salt (0·5 g.) in warm acetic acid (250 ml.) was diluted to 500 ml. with chloroform and allowed to percolate down a column (60 cm. × 2 cm.) of Amberlite IR-120 resin during 2 hr. The eluant, together with 100 ml. of washings, was concentrated to dryness *in vacuo*, and the residue (0·43 g., 92%), m. p. 75—76°, was shown to be hexadecyl dihydrogen phosphate by its *X*-ray powder photograph.

Didodecyl Hydrogen Phosphate.—Phenyl phosphorodichloridate (4·2 g., 0·02 mole) was added dropwise to a warm solution of dodecan-1-ol (7·4 g., 0·04 mole) in dry pyridine (15 ml.). The solution was kept for 48 hr., after which it was poured into N-hydrochloric acid (200 ml.), and the precipitated oil was extracted with ether. The ethereal solution was washed with N-hydrochloric acid (3 times), 5% sodium hydrogen carbonate (5 times), and water (5 times), and dried (Na_2SO_4). The ether was then removed at 20 mm. and traces of pyridine at 0·5 mm. pressure.

The residual oil (9·9 g.) was dissolved in glacial acetic acid (100 ml.), and after the addition of platinic oxide (Adams; 0·5 g.), the solution was shaken in hydrogen until absorption ceased (3 hr.; 1600 ml.). The catalyst was filtered off and washed with chloroform, and the solvents were removed from the filtrate *in vacuo*. The residue, crystallised from methanol, yielded didodecyl hydrogen phosphate (5·9 g., 70%) as soft white plates, m. p. 59° (Found : C, 66·3; H, 11·7; P, 7·0%; equiv., 432. $C_{24}H_{51}O_4P$ requires C, 66·3; H, 11·8; P, 7·2%; equiv., 435).

The following were prepared identically :

Dioctadecyl hydrogen phosphate (84%), m. p. 82° (Found : C, 71·9; H, 12·4; P, 5·1%; equiv., 599. $C_{36}H_{75}O_4P$ requires C, 71·7; H, 12·6; P, 5·2%; equiv., 603).

Dihexadecyl hydrogen phosphate (80%), m. p. 75° (Found : C, 70·3; H, 12·1; P, 6·1%; equiv., 542. $C_{32}H_{67}O_4P$ requires C, 70·3; H, 12·4; P, 5·7%; equiv., 547).

Ditetradecyl hydrogen phosphate (74%), m. p. 68° (Found : C, 68·8; H, 12·0; P, 6·5%; equiv., 497. $C_{28}H_{59}O_4P$ requires C, 68·4; H, 12·2; P, 6·3%; equiv., 491).

Sodium Dioctadecyl Phosphate. Dioctadecyl phosphate (0·6 g.) was dissolved in warm ethanol (20 ml.), and 0·1N-sodium hydroxide solution (10 ml.) was added. After cooling, the precipitated *sodium salt* was filtered off, and washed with ethanol and ether (yield, 0·58 g.; colourless flakes) (Found : C, 69·0; H, 11·4; P, 4·6. $C_{36}H_{74}O_4PNa$ requires C, 69·2; H, 11·7; P, 4·9%).

The following were made in a similar manner :

Sodium dihexadecyl phosphate (Found : C, 67·4; H, 11·7; P, 5·0. $C_{32}H_{66}O_4PNa$ requires C, 67·6; H, 11·7; P, 5·4%).

Sodium ditetradecyl phosphate (Found : C, 65·3; H, 11·3; P, 6·15. $C_{28}H_{58}O_4PNa$ requires C, 65·5; H, 11·5; P, 6·1%).

Sodium didodecyl phosphate (Found : C, 62·9; H, 11·1; P, 6·9. $C_{24}H_{50}O_4PNa$ requires C, 63·0; H, 11·1; P, 6·8%).

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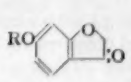
Survey of Anthoxanthins. Part IX. Isolation and Constitution of Palasitrin.*

By (Miss) B. Puri and T. R. Seshadri.

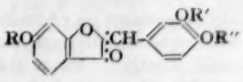
[Reprint Order No. 6020.]

A new glycoside, palasitrin, has been isolated from the flowers of *Butea frondosa*. It yields on hydrolysis 2 mols. of glucose and 2-(3 : 4-dihydroxybenzylidene)-6-hydroxycoumaran-3-one. The glucose units are in the 6- and the 3′-position since, on complete methylation and hydrolysis, the glycoside yields the 4′-monomethyl ether of the aglycone. For comparison all the monomethyl ethers of the aglycone have been synthesised. Butein and *iso*butrin have been converted into the aglycone and palasitrin by acetylation, addition of bromine, and treatment with alcoholic alkali.

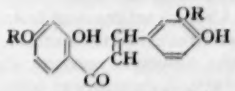
In Part III (Puri and Seshadri, *J. Sci. Ind. Res. India*, 1953, **12**, *B*, 462) were described the isolation and study of *iso*butrin, a new butein glycoside from the dried flowers of *Butea frondosa*. The existence of butrin (butin diglucoside) along with small amounts of the aglycones, butin and butein, had been recorded in earlier publications. Extraction of the fresh flowers with cold alcohol and chromatography showed the presence of *iso*butrin as almost the sole glycosidic component, butrin and the aglycones being absent. There was very little carotene in the flowers, but the deep orange-red colour suggested the presence of another pigment. After the removal of butrin (formed during the concentration) and *iso*butrin from the alcoholic extract by fractional crystallisation, the mother-liquors yield a brownish-red, crystalline pigment, $C_{27}H_{30}O_{15}$, which is named palasitrin, derived from the Indian name of the tree, Palas. On hydrolysis with acid this gives two mols. of glucose and one of an aglycone identified as 2-(3 : 4-dihydroxybenzylidene)-6-hydroxycoumaran-3-one (II; R = R′ = R″ = H) by comparison with a sample prepared by a modification of the method of Bruhl and Friedlander (*Ber.*, 1897, **30**, 297) and von Auwers and Pohl (*Annalen*, 1914, **405**, 243). Further, 6-hydroxycoumaran-3-one (I; R = H) was condensed with vanillin, and the 3′-methyl ether (II; R = R″ = H, R′ = Me) completely methylated, yielding the trimethyl ether of the aglycone.



(I)



(II)



(III; R = $C_6H_{11}O_6$)

When completely methylated and then hydrolysed, the glycoside gave a monomethyl ether, m. p. 241—243°, showing that the two glucose units were in different positions. It differed from the 3′-methyl ether already mentioned, and from the 6-methyl ether (m. p. 223—225°) obtained by the condensation of 6-methoxycoumaran-3-one (I; R = Me) with protocatechuic aldehyde, but resembled the 4′-methyl ether (II; R = R′ = H, R″ = Me) (m. p. 241—243°) prepared from 6-hydroxycoumaran-3-one and *iso*vanillin. Palasitrin is therefore the 6 : 3′-diglucoside. The fact that the positions occupied by the sugar units in this glycoside and in *iso*butrin (III) are similar is of significance: it appears that *iso*butrin undergoes oxidation to palasitrin or that they have a common origin. In the laboratory the conversion of a chalkone into a benzylidenecoumaranone is fairly easy: butein tetra-acetate yields its dibromide which gives the aglycone (II; R = R′ = R″ = H) on treatment with alcoholic potassium hydroxide. By the same procedure *iso*butrin was converted into palasitrin.

By chromatography it was shown that flowers, and particularly buds, collected at the beginning of the season contain only *iso*butrin whereas later a considerable quantity of palasitrin was present in the mature flowers. The occurrence of benzylidenecoumaranones along with chalkones or flavanones has been noted, *e.g.*, leptosin in *Coreopsis grandiflora*

* Part VIII, *J. Sci. Ind. Res. India*, 1955, **14**, *B*, 93.

(Geissman and Heaton, *J. Amer. Chem. Soc.*, **1943**, **65**, 677), aureusin in *Antirrheinum majus* (Seikel and Geissman, *ibid.*, **1950**, **72**, 5725), 6 : 3′ : 4′-trihydroxyaurone in yellow *Dahlia* (Nordstrom and Swain, *Chem. and Ind.*, **1953**, 823), and sulphurein in *Cosmos sulphureus* (Shimokariyama and Hattori, *J. Amer. Chem. Soc.*, **1953**, **75**, 1900).

Experimental

For circular paper chromatography Whatman No. 1 paper and water saturated with phenol at 34—36° were used.

Extraction of Fresh Flowers.—(a) *Chromatography of the extracts.* The orange-red fully grown flowers were extracted with cold alcohol for 2 days. The process was repeated twice with fresh alcohol. In circular paper chromatography it gave a marked orange-yellow ring without spraying, R_F 0·72, which corresponds to *iso*butrin. Another yellow ring was present which when sprayed with ammonia became purple (R_F 0·65). No rings corresponding to butein, butrin, or butin appeared. Similar extractions were carried out with the following materials : (1) Fresh buds collected in the beginning of the season gave only *iso*butrin. (2) Flowers air-dried indoors gave the same results as fresh flowers. (3) Sun-dried flowers gave two yellow rings, as with fresh flowers before spraying, but a third yellow ring (R_F 0·87) appeared after spraying, which corresponded to butrin. Thus sun-drying caused some conversion of *iso*butrin into butrin. (4) Extracts of fresh flowers concentrated under ordinary pressure gave results similar to those last noted, showing the effect of evaporation at atmospheric pressure.

(b) *Butrin.* The alcoholic extract of the flowers was concentrated at atmospheric pressure to a small volume and set aside. An orange-yellow crystalline solid separated. After two crystallisations from methyl alcohol and one from alcohol it formed colourless long needles, m. p. 194—195° (decomp.). It gave no colour with alcoholic ferric chloride and a deep pink colour with magnesium and hydrochloric acid. In paper chromatography no ring was visible before spraying and only after spraying with ammonia a yellow ring, R_F 0·87, appeared. This fraction was therefore butrin (Puri and Seshadri, *loc. cit.*).

(c) iso*Butrin.* The mother-liquor after removal of butrin was further concentrated and cooled. Bright yellow crystals were obtained which crystallised from methyl alcohol as small narrow prisms and needles, m. p. 190—191° (decomp.) after sintering at 185°. In paper chromatography the substance gave a marked yellow ring before spraying with ammonia (R_F 0·72). It gave an olive-brown colour with alcoholic ferric chloride but no colour with magnesium powder and hydrochloric acid. These properties agreed with those of *iso*butrin (Puri and Seshadri, *loc. cit.*).

A rough estimate of *iso*butrin was made by exhaustion of fresh flowers (150 g.) with alcohol, concentration of the extract, hydrolysis with aqueous sulphuric acid (7%), and ether-extraction of the aglycone mixture (butin and butein mostly). From the yield of the dry aglycone mixture, *iso*butrin was found to constitute 5% of the fresh flowers and 25% of the air-dried flowers.

(d) *Palasitrin.* The mother-liquor from *iso*butrin was extracted repeatedly with ether, to remove any free aglycones. The aqueous layer was then saturated with ammonium sulphate and extracted with butyl alcohol. The extract was diluted with light petroleum and then extracted with small portions of aqueous 5% potassium carbonate. The carbonate extract was acidified in the cold and re-extracted with butyl alcohol. This alcohol extract was then evaporated, and the residue dissolved in methanol (50 c.c.) and passed down a column of magnesol (30 × 1·5 cm.) under suction to remove the last traces of *iso*butrin. *iso*Butrin formed the lower yellow zone and palasitrin an upper orange-red zone. The zones were then washed down with methyl alcohol, the extract of the new glycoside concentrated, and the residue recrystallised from butyl alcohol; it formed long prisms, m. p. 199—200° (decomp.) after sintering at 125° (Found : C, 53·3; H, 5·6; loss on drying at 110°, 2·9. $C_{27}H_{30}O_{15}.H_2O$ requires C, 52·9; H, 5·2; H_2O, 3·0%). It gave a purple solution with aqueous sodium hydroxide, a deep-red solution with concentrated sulphuric acid, an olive-brown colour with alcoholic ferric chloride, and no colour with magnesium powder and hydrochloric acid. In paper chromatography it gave a yellow ring which became purple when sprayed with ammonia (circular R_F 0·66). The yield of palasitrin was approx. 0·2% of the fresh flowers.

Hydrolysis of Palasitrin.—The glycoside was boiled with 7% aqueous-alcoholic sulphuric acid for 2 hr. When the solution was cooled an orange-yellow solid separated which in paper chromatography gave a yellow ring becoming purple-red when sprayed with ammonia (R_F 0·45). The *aglucone* crystallised from alcohol as deep orange-yellow prisms, m. p. 310—312° (decomp.), gave

an olive-brown colour with alcoholic ferric chloride, no colour with magnesium and hydrochloric acid, an orange-red colour with concentrated sulphuric acid, and a purple-red colour with aqueous sodium hydroxide (Found: C, 67·0; H, 4·0. $C_{15}H_{10}O_5$ requires C, 66·7; H, 3·7%). The mixed m. p. with a synthetic sample was undepressed.

The aqueous solution was finally extracted with ether to remove the last traces of the aglucone and neutralised with barium carbonate. The solution was filtered off, concentrated and tested for sugar {circular R_F 0·60; 34—36°; phenol–water (9 : 1); indicates glucose [Found: glucose, 58·5; aglucone, 44·4. $C_{27}H_{30}O_{15}.H_2O$ requires glucose (2 mols.), 58·8; aglucone, 44·1]}.

The aglucone trimethyl ether, prepared by methyl sulphate and potassium carbonate in boiling acetone (20 hr.), crystallised from dilute alcohol as colourless rectangular prisms and plates, m. p. 184—186°, alone or mixed with a synthetic sample.

Synthesis of 2-(3 : 4-*Dimethoxybenzylidene*)-6-*hydroxycoumaran*-3-*one*.—(a) 6-*Hydroxy*-2-(4-*hydroxy*-3-*methoxybenzylidene*)*coumaran*-3-*one*. A solution of 6-hydroxycoumaran-3-one (Balakrishna, Rao, and Seshadri, *Proc. Indian Acad. Sci.*, 1949, **29**, *A*, 399) (2 g.) and vanillin (4 g.) in alcohol (20 c.c.) was treated with 30 c.c. of aqueous potassium hydroxide (50 g. in 35 c.c.) and kept at room temperature for 3 days with occasional shaking, then diluted with water, and acidified with hydrochloric acid. The *monomethyl ether* crystallised from dilute alcohol as yellow rectangular prisms, m. p. 263—264° (Found, in the sample dried at 120° *in vacuo*: C, 67·5; H, 4·0. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%).

(b) *Methylation*. The monomethyl ether was heated in acetone with an excess of methyl sulphate and potassium carbonate for 12 hr. The *trimethyl ether*, crystallised twice from dilute alcohol, yielded colourless rectangular prisms and plates, m. p. 184—186° (Found: C, 69·2; H, 5·5. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·1%).

Complete Methylation and Hydrolysis of Palasitrin.—Palasitrin (0·5 g.) was heated in dry acetone (100 c.c.) with methyl sulphate (1·5 c.c.) and potassium carbonate (3 g.) for 30 hr. Acetone was then distilled off, and water added to dissolve the potassium salts and enough sulphuric acid to neutralise the carbonate and to make the acid strength 7%. The mixture was boiled for 2 hr., cooled, and extracted with ether. Evaporation yielded a yellow solid which crystallised from alcohol as orange-yellow prismatic needles and rods, m. p. 241—242° alone or mixed with synthetic 6-*hydroxy*-2-(3-*hydroxy*-4-*methoxybenzylidene*)*coumaran*-3-*one* (Found: C, 60·5; H, 4·5; loss at 120°, 10·5. $C_{16}H_{12}O_5.2H_2O$ requires C, 60·0; H, 5·0; H_2O, 11·2%. Found in the sample dried at 120°: OMe, 10·7. $C_{16}H_{12}O_5$ requires OMe, 10·9%).

Synthesis. Condensation of 6-hydroxycoumaran-3-one (1 g.) with *iso*vanillin (2 g.) was effected as with vanillin. The 4′-methyl ether crystallised from alcohol as orange-yellow prismatic needles and rods, m. p. 241—243° (Found, in the sample dried at 120°: OMe, 10·8. $C_{16}H_{12}O_5$ requires for 1OMe, 10·9%).

Synthesis of 2-(3 : 4-*Dihydroxybenzylidene*)-6-*hydroxycoumaran*-3-*one*.—The following modified procedure has been found convenient. A solution of 6-hydroxycoumaran-3-one (1·50 g.) and protocatechualdehyde (1·38 g.) in alcohol (20 c.c.) was saturated with hydrogen chloride (ice-cooling) in 2 hr., then diluted with water and extracted with ether. The solvent was evaporated off and the solid twice crystallised from alcohol, yielding orange-yellow prisms, m. p. 310—312° (decomp.).

2-(3 : 4-*Dihydroxybenzylidene*)-6-*methoxycoumaran*-3-*one*.—6-Methoxycoumaran-3-one (Balakrishna, Rao, and Seshadri, *loc. cit.*) (1·64 g.) was condensed with protocatechuic aldehyde (1·38 g.) as in the foregoing experiment. After two crystallisations from dilute alcohol the *product* formed red prisms, m. p. 223—225°. The solution in alcohol was yellow but the crystalline solid deep red (Found: C, 68·3; H, 4·7. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%).

Conversion of Butein into 2-(3 : 4-*Dihydroxybenzylidene*)-6-*hydroxycoumaran*-3-*one*.—(*a*) Butein tetra-acetate (Perkin and Everest, "Natural Organic Colouring Matters," Longmans, London, 1918, p. 169) (0·5 g.) in glacial acetic acid (5 c.c.) was treated dropwise with bromine in acetic acid. The mixture was cooled in ice and the orange-yellow solid *dibromide* which separated was filtered off and washed with water. It crystallised from acetone–light petroleum as pale red prisms, m. p. 86—88° (Found: Br, 25·6. $C_{23}H_{20}O_9Br_2$ requires Br, 26·7%).

(*b*) The crude dibromide was boiled with aqueous 10% potassium hydroxide (50 c.c.) until the whole was a clear solution (10 min.), cooled, acidified with hydrochloric acid, and extracted with ether. The solvent was evaporated and the residue tested chromatographically. It gave a marked yellow ring (R_F 0·45) which became purple when sprayed with ammonia. Another ring which appeared pale yellow only after spraying with ammonia (R_F 0·56) indicated a minor by-product, probably a flavone. The solid was repeatedly recrystallised from ethyl acetate till

a pure sample was obtained having m. p. 310—312° (decomp.) alone or mixed with the sample obtained by the hydrolysis of palasitrin.

Conversion of iso*Butrin into Palasitrin.*—*iso*Butrin (1 g.) was heated with acetic anhydride (15 c.c.) and sodium acetate (3 g.) for 3 hr., and then poured into ice-water. The product, crystallised repeatedly from alcohol, yielded *isobutrin acetate* as pale yellow rectangular prisms, m. p. 108—110° (Found: C, 56·0; H, 5·6. $C_{47}H_{38}O_{18}$ requires C, 55·5; H, 5·1%).

To the acetate (0·5 g.) in glacial acetic acid (5 c.c.) bromine in glacial acetic acid was added dropwise. Water was added and the resulting orange-yellow sticky solid filtered off and boiled with aqueous 10% potassium hydroxide (50 c.c.) until completely dissolved. The solution was cooled, acidified with hydrochloric acid, and extracted with butyl alcohol, and the extract concentrated. The residue gave in chromatography a yellow ring (R_F 0·64), becoming purple when sprayed with ammonia. It was purified by column chromatography as for natural palasitrin. The pure product crystallised from butyl alcohol as long prisms, m. p. 199—200° (decomp.) with sintering at 125°, alone or mixed with the natural sample. There was agreement in all colour reactions.

UNIVERSITY OF DELHI, DELHI-8. [*Received, January 8th*, 1955.]

The Synthesis and Reactions of Branched-chain Hydrocarbons. Part VII. The Preparation and Pinacol Rearrangement of Some αβ-Acetylenic Ditertiary Glycols.*

By M. F. ANSELL, W. J. HICKINBOTTOM, and A. A. HYATT.

[Reprint Order No. 6085.]

The preparation of three αβ-acetylenic ditertiary glycols is described, and the action of concentrated sulphuric acid at −20° on two of them reported.

αβ-ACETYLENIC ditertiary glycols (II) have been previously prepared by the action of acetylene on α-hydroxy-ketones (I) in ether in the presence of either potassium hydroxide (Favorski and Onischenko, *J. Gen. Chem. U.S.S.R.*, 1941, **11**, 1111) or sodamide (Bernard and Colonge, *Bull. Soc. chim. France*, 1945, **12**, 347). We have now found, in agreement with Davis and Erman (*J. Amer. Chem. Soc.*, 1954, **76**, 3477; published since the completion of this work) that these compounds may be prepared in good yield, in some cases, by the use of sodium acetylide in liquid ammonia. Thus 3-hydroxy-3-methylbutan-2-one (I; R = R′ = Me) and 3-hydroxy-3 : 5 : 5-trimethylhexan-2-one (I; R = Me, R′ = $CMe_3 \cdot CH_2$) yield respectively 2 : 3-dimethylpent-4-yne-2 : 3-diol (II; R = R′ = Me) and

(I) HO·CRR′·COMe HO·CRR′·CMe(OH)·C≡CH (II)

3 : 4 : 6 : 6-tetramethylhept-1-yne-3 : 4-diol (II; R = Me, R′ = $Me_3C \cdot CH_2$) in good yield, while a poorer yield of 3 : 4 : 4 : 5-tetramethylhex-1-yne-3 : 4-diol (II; R = Me, R′ = Bu^t) was obtained from 3-hydroxy-3 : 4 : 4-trimethylpentan-2-one (I; R = Me, R′ = Bu^t). The yield was not improved by the use of lithium acetylide or by employing boiling ether or benzene as solvent. 3-Hydroxy-4-methyl-3-*iso*propylpentan-2-one (I; R = R′ = Pr^i) and 3-hydroxy-3 : 4 : 4 : 6 : 6-pentamethylheptan-2-one (I; R = Me, R′ = $Me_3C \cdot CH_2 \cdot CMe_2$) failed to react with acetylene under any of the above conditions. The structure of each of the αβ-acetylenic glycols prepared was proved by oxidation with periodic acid to but-3-yn-2-one and a saturated ketone.

The pinacol rearrangement of 2 : 3-dimethylpent-4-yne-2 : 3-diol (III) has been reported by Favorski and Onischenko (*loc. cit.*) to yield 3 : 3-dimethylpentane-2 : 4-dione (VI) in concentrated sulphuric acid at −10° and, subsequent to this work, Davis and Erman (*loc. cit.*) reported that 3 : 3-dimethylpent-4-yn-2-one (V) is produced in the presence of boiling 40% sulphuric acid. We have found that both these products, together with 3-methylbutan-2-one, arise if the rearrangement is performed in concentrated sulphuric acid

* Part VI, *J.*, 1955, 349.

at −20°. We consider that 3 : 3-dimethylpentane-2 : 4-dione (VI) arises by the initial hydration of the ethynyl group of the glycol followed by the rearrangement of the dihydroxy-ketone (IV) produced, as we have been unable to hydrate the ethynyl group of 3 : 3-dimethylpent-4-yn-2-one.

(III) $HO{\cdot}CMe_2{\cdot}CMe(OH){\cdot}C{\equiv}CH$ $HO{\cdot}CMe_2{\cdot}CMe(OH){\cdot}COMe$ (IV)

(V) $Me{\cdot}CO{\cdot}CMe_2{\cdot}C{\equiv}CH$ $Me{\cdot}CO{\cdot}CMe_2{\cdot}COMe$ (VI)

The rearrangement of 3 : 4 : 6 : 6-tetramethylhept-1-yne-3 : 4-diol (VII) in concentrated sulphuric acid at −20° gave small amounts of 4 : 4-dimethylpentan-2-one and but-3-yn-2-one, which appear to arise by fission of the glycol (cf. Hickinbottom, Hyatt, and Sparke, *J.*, 1954, 2533; Hickinbottom and Pyle, unpublished work). The principal products were the normal rearrangement product, 2 : 2 : 5 : 5-tetramethylhept-6-yn-4-one (IX) (identified by conversion into 2 : 2 : 5 : 5-tetramethylheptan-4-ol), 3 : 5 : 5-trimethylhexan-2-one, and 3 : 4 : 6 : 6-tetramethylhepta-2 : 4-dien-1-al (X). The latter, identified by ozonolysis, may arise through a Meyer–Schuster–Rupe type of rearrangement (A. W. Johnson, "The Chemistry of Acetylenic Compounds," Edward Arnold & Co., London, 1946, Vol I, pp. 124—130), followed by dehydration of the intermediate unsaturated hydroxy-aldehyde

(VII) $Me_3C{\cdot}CH_2{\cdot}CMe(OH){\cdot}CMe(OH){\cdot}C{\equiv}CH$ $Me_3C{\cdot}CH_2{\cdot}CMe(OH){\cdot}CMe{:}CH{\cdot}CHO$ (VIII)

(IX) $Me_3C{\cdot}CH_2{\cdot}CO{\cdot}CMe_2{\cdot}C{\equiv}CH$ $Me_3C{\cdot}CH{:}CMe{\cdot}CMe{:}CH{\cdot}CHO$ (X)

(VIII). This type of rearrangement has been previously observed in the action of sulphuric acid on 2 : 3-dimethyl-5-phenylpent-4-yne-2 : 3-diol (XI) which gives 2-hydroxy-2 : 3-dimethyl-5-phenylpent-3-en-5-one (XII) and 2 : 3-dimethyl-5-phenylpenta-1 : 3-dien-5-one (XIII) in addition to the " normal " product (Venus-Danilova, Serkova, and Pavlova, *J. Gen. Chem. U.S.S.R.*, 1951, **21**, 2210).

$HO{\cdot}CMe_2{\cdot}CMe(OH){\cdot}C{\equiv}CPh$ (XI) $HO{\cdot}CMe_2{\cdot}CMe{:}CH{\cdot}COPh$ (XII) $CH_2{:}CMe{\cdot}CMe{:}CH{\cdot}COPh$ (XIII)

The mechanism of the formation, in both of the above rearrangements, of a saturated ketone containing two fewer carbon atoms than the original glycols is a matter of speculation. The subject is under investigation and will be reported later.

Experimental

Preparation of α-Hydroxy-ketones.—(*A*) 3-Hydroxy-3-methylbut-1-yne (Froning and Hennion, *J. Amer. Chem. Soc.*, 1940, **62**, 653) (420 g.) was added during 3 hr. to a vigorously stirred boiling solution of mercuric oxide (7·5 g.) in sulphuric acid (30 g.) and water (500 c.c.), with continuous steam-distillation. The distillate was saturated with sodium chloride, and the upper layer separated and combined with the ethereal extract of the aqueous layer and dried ($MgSO_4$). Distillation gave, after a small forerun, 3-hydroxy-3-methylbutan-2-one (449 g., 88%), b. p. 140—142°, n_D^{20} 1·4150, which yielded a 2 : 4-*dinitrophenylhydrazone*, m. p. 149°, orange needles from benzene–light petroleum (Found : C, 47·0; H, 5·0; N, 20·0. $C_{11}H_{14}O_5N_4$ requires C, 46·8; H, 5·0; N, 19·9%), and a semicarbazone, m. p. 164° (from ethanol). Froning and Hennion (*loc. cit.*) record b. p. 139°, n_D^{20} 1·4150. Scheibler and Fischer (*Ber.*, 1922, **55**, 2903) record a semicarbazone, m. p. 164°.

(*B*) 3-Hydroxy-3 : 4 : 4-trimethylpentan-2-one, 3-hydroxy-3 : 5 : 5-trimethylhexan-2-one, 3-hydroxy-4-methyl-3-*iso*propylpentan-2-one, and 3-hydroxy-3 : 4 : 4 : 6 : 6-pentamethylheptan-2-one were prepared by the method of Hickinbottom, Hyatt, and Sparke (*J.*, 1954, 2529).

Preparation of αβ-Acetylenic Glycols.—The α-hydroxy-ketone (1·5 moles) was added dropwise during 3 hr. to a well-stirred suspension of sodium acetylide (3·0 moles) in liquid ammonia (2 l.) through which a slow stream of acetylene was passing. After 1 hour's stirring the acetylene was shut off and ammonium chloride (200 g.) added. After further stirring (1 hr.) the ammonia was allowed to evaporate overnight. Water (2 l.) was added, and the mixture extracted with ether (10 × 100 c.c.). Distillation of the dried ($MgSO_4$) ethereal extract gave, after a small forerun, the αβ-acetylenic glycol. Thus were prepared : 2 : 3-dimethylpent-4-yne-2 : 3-diol (151 g.), b. p. 82—84°/13 mm., n_D^{20} 1·4626 (Davis and Erman, *loc. cit.*, record b. p. 90—91°/19

mm., n_D^{22} 1·4600), 3 : 4 : 6 : 6-*tetramethylhept*-1-*yne*-3 : 4-*diol* (221 g.), b. p. 76—78°/1·5 mm., n_D^{20} 1·4650 (Found : C, 71·8; H, 10·9. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%), and 3 : 4 : 5 : 5-tetramethylhex-1-yne-3 : 4-diol (13·6 g.; 183·4 g. of α-hydroxy-ketone recovered), b. p. 70—71°/0·9 mm., n_D^{20} 1·4751, m. p. 54—56° (Bernard and Colonge, *loc. cit.*, record b. p. 104—107°/15 mm., n_D^{13} 1·4748). No reaction occurred with 3-hydroxy-4-methyl-3-*iso*propylpentan-2-one or 3-hydroxy-3 : 4 : 4 : 6 : 6-pentamethylheptan-2-one under the above conditions or with sodium or lithium acetylide in boiling ether or benzene, nor could the yield of 3 : 4 : 5 : 5-tetramethylhex-1-yne-3 : 4-diol be improved by using these modifications.

Oxidative Fission of the αβ-Acetylenic Glycols.—Periodic acid (3 g.) was added to a solution of the glycol (3 g.) in aqueous methanol (20 c.c.), and the mixture shaken (3 hr.). Air was then aspirated through the solution for 3 hr. and passed into a warm solution of 2 : 4-dinitrophenylhydrazine in aqueous-alcoholic sulphuric acid. The precipitate formed was filtered off, dried, and chromatographed in benzene–light petroleum (b. p. 60—80°) (1 : 9) through alumina. Elution with the same solvent gave, in the case of 2 : 3-dimethylpent-4-yne-2 : 3-diol, the 2 : 4-dinitrophenylhydrazone of acetone (m. p. and mixed m. p. 125°) and, in the case of 3 : 4 : 6 : 6-tetramethylhept-1-yne-3 : 4-diol, the 2 : 4-dinitrophenylhydrazone of 4 : 4-dimethylpentan-2-one (m. p. and mixed m. p. 101°). Further elution, with the same solvent plus 10% of ether, gave, in each case, the 2 : 4-dinitrophenylhydrazone of but-3-yn-2-one, m. p. 180°. Bowden, Heilbron, Jones, and Weedon (*J.*, 1946, 39) record m. p. 181°.

Rearrangement of 2 : 3-*Dimethylpent*-4-*yne*-2 : 3-*diol.*—The glycol (100 g.) was added dropwise during 2 hr. to concentrated sulphuric acid (1200 g.) kept at −20°. After about 10 g. of glycol had been added the mixture liquefied and efficient stirring was commenced and continued throughout the addition and for 1 hr. subsequently. The pale yellow syrup was then poured on crushed ice (4 kg.), water (4 l.) added, and the mixture steam-distilled. The organic layer of the distillate was separated, and the aqueous layer extracted with ether. The combined organic material was washed with a little water and dried ($MgSO_4$), and the ether removed. Fractional distillation of the residue gave fractions :

Fraction	B. p.	Wt. (g.)	n_D^{20}	Fraction	B. p.	Wt. (g.)	n_D^{20}
1	<92°	1·4	1·3802	5	117—119°	39·5	1·4206
2	92—100	9·2	1·3877	6	—55°/13 mm.	0·9	1·4284
3	100—105	1·5	1·3982	7	55—60°/13 mm.	11·6	1·4332
4	105—117	5·2	1·4182		Residue	1·3	—

Fraction 1 was unsaturated but no pure component could be isolated. Refractionation of fraction 2 gave 3-methylbutan-2-one, b. p. 94°, n_D^{20} 1·3875 (semicarbazone, m. p. and mixed m. p. 112—113°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 117°). Fraction 5 gave a white precipitate with ammoniacal silver nitrate and on redistillation gave 3 : 5-dimethylpent-4-yn-2-one, b. p. 117—118°, n_D^{20} 1·4202 (Found : C, 76·2; H, 9·2. Calc. for $C_7H_{10}O$: C, 76·3; H, 9·2%) [2 : 4-dinitrophenylhydrazone, yellow needles (from ethanol), m. p. 140°; *semicarbazone*, needles (from ethanol), m. p. 130° (Found : C, 57·6; H, 8·1; N, 24·9. $C_8H_{13}ON_3$ requires C, 57·5; H, 7·8; N, 25·1%). Davis and Erman (*loc. cit.*) record b. p. 117·5°, n_D^{25} 1·4180, 2 : 4-dinitrophenylhydrazone, m. p. 139°. Hydrogenation of 3 : 5-dimethylpent-4-yn-2-one in alcohol with Adams's catalyst at 50 lb./sq. in. gave 3 : 3-dimethylpentan-2-one, b. p. 128—130°, n_D^{20} 1·4101 (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 112°; semicarbazone, m. p. and mixed m. p. 136°).

Fraction 7, when distilled, yielded 3 : 3-dimethylpentane-2 : 4-dione, b. p. 173°, n_D^{20} 1·4332, which gave a *disemicarbazone* (purified by boiling with ethanol, benzene, and ether), m. p. and mixed m. p. 220° (Found : C, 44·6; H, 7·2; N, 34·5. $C_9H_{18}O_2N_6$ requires C, 44·6; H, 7·5; N, 34·7%), and a *bis*-2 : 4-*dinitrophenylhydrazone*, orange plates (from ethanol), m. p. and mixed m. p. 146° (Found : C, 46·9; H, 4·1; N, 22·8. $C_{19}H_{20}O_8N_8$ requires C, 46·7; H, 4·1; N, 22·9%). The authentic specimens were obtained from the dione prepared according to Kohler and Erickson (*J. Amer. Chem. Soc.*, 1931, 53, 2301).

Rearrangement of 3 : 4 : 6 : 6-*Tetramethylhept*-1-*yne*-3 : 4-*diol.*—The glycol (215 g.) was rearranged as for the previous example but with concentrated sulphuric acid (1500 c.c.; 2757 g.). Fractional distillation of the organic material gave 5·3 g. in the cold trap, (*a*) 16·4 g. of b. p. <78°/19 mm., n_D^{20} 1·4271—1·4471, (*b*) 40·1 g. of b. p. 78—102°/19 mm., n_D^{20} 1·4540—1·4595, and 35·2 g. of residue. All the fractions were unsaturated and had olefinic odours. Material (*a*) was treated with excess of an aqueous-ethanolic solution of semicarbazide hydrochloride and sodium acetate. The solid precipitated overnight was recrystallised from ethanol and hydrolysed by boiling 20% aqueous oxalic acid. The organic material was extracted with

ether, washed with aqueous sodium carbonate solution, and water, and dried ($MgSO_4$). Distillation gave **3 : 5 : 5-trimethylhexan-2-one** (10·9 g.), b. p. 61°/19 mm., n_D^{20} 1·4172 (Found : C, 76·2; H, 12·5. Calc. for $C_9H_{18}O$: C, 76·0; H, 12·7%) [semicarbazone, needles (from ethanol), m. p. 177°; 2 : 4-dinitrophenylhydrazone, yellow plates (from ethanol), m. p. 65°]. Whitmore and Meunier (*J. Amer. Chem. Soc.*, **1941**, **63**, 2197) record semicarbazone, m. p. 168—169°, and 2 : 4-dinitrophenylhydrazone, m. p. 63—64°. Colonge and Dreux (*Compt. rend.*, **1950**, **230**, 1776) record ketone, b. p. 61°/19 mm., and semicarbazone, m. p. 176°.

Material (*b*) was purified *via* the semicarbazone as above to yield **2 : 2 : 5 : 5-tetramethylhept-6-yn-4-one** (16·4 g.), b. p. 90°/16 mm., n_D^{20} 1·4652 (Found : C, 79·2; H, 11·2. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%), which gave a *semicarbazone*, needles (from ethanol), m. p. 206° (Found : C, 64·2; H, 9·2; N, 18·9. $C_{12}H_{21}ON_3$ requires C, 64·5; H, 9·5; N, 18·8%), and a 2 : 4-*dinitrophenylhydrazone*, yellow crystals (from ethanol), m. p. 124° (Found : C, 58·8; H, 6·6; N, 16·3. $C_{17}H_{22}O_4N_4$ requires C, 58·9; H, 6·4; N, 16·2%). Hydrogenation of **2 : 2 : 5 : 5-tetramethylhept-6-yn-4-one** in alcohol with Adams's catalyst at 50 lb./sq. in. followed by reduction of the product with lithium aluminium hydride gave **2 : 2 : 5 : 5-tetramethylheptan-4-ol**, b. p. 85°/14 mm., n_D^{20} 1·4410 [3 : 5-dinitrobenzoate (from light petroleum, b. p. 40—60°), m. p. and mixed m. p. 108°]. The preparation of this alcohol will be described in Part IX.

The residue was further distilled and all the fractions from it were unsaturated, but none gave a precipitate with ammoniacal silver nitrate. The carbonyl fractions, b. p. 65—100°/2 mm., n_D^{20} 1·4600—1·4770, were treated with excess of aqueous-alcoholic semicarbazide hydrochloride and sodium acetate. The precipitate which was rapidly formed was filtered off, purified by boiling it with ether, and then hydrolysed by shaking it in light petroleum (b. p. 40—60°) for 24 hr. with 20% sulphuric acid. Distillation of the washed (sodium carbonate solution, and water) and dried ($MgSO_4$) ethereal extract gave **3 : 4 : 6 : 6-tetramethylhepta-2 : 4-dien-1-al** (9·3 g.), b. p. 75°/2 mm., n_D^{20} 1·4861, which reduced Fehling's solution but not Schiff's reagent and darkened and became viscous on storage (Found : C, 79·5; H, 11·0. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%), and gave a *semicarbazone* (purified by extraction with ethanol, benzene, and ether), m. p. 238° (Found : C, 64·5; H, 9·5; N, 18·8. $C_{12}H_{21}ON_3$ requires C, 64·5; H, 9·5; N, 18·8%), and a 2 : 4-*dinitrophenylhydrazone*, scarlet crystals [from benzene-light petroleum (b. p. 60—80°)], m. p. 178° (Found : C, 58·9; H, 6·4; N, 16·0. $C_{17}H_{22}O_4N_4$ requires C, 58·9; H, 6·4; N, 16·2%). Ozonolysis of **3 : 4 : 6 : 6-tetramethylhepta-2 : 4-dienal** in chloroform gave trimethylacetaldehyde and diacetyl which were isolated as the 2 : 4-dinitrophenylhydrazones, m. p.s and mixed m. p.s 210° and 243° respectively, the separation being effected by chromatography on alumina from light petroleum–benzene–ether (9 : 1 : 1).

Material from the cold trap, on redistillation, gave (*A*) **but-3-yn-2-one**, b. p. 80—86°, n_D^{20} 1·4050 [2 : 4-dinitrophenylhydrazone, yellow needles (from ethanol), m. p. 180°] [Bowden *et al.* (*loc. cit.*) record b. p. 84·5—86°, n_D^{22} 1·4050 (2 : 4-dinitrophenyhydrazone, m. p. 181°)], and (*B*) a liquid, b. p. 110—125°, n_D^{20} 1·4043. The latter was treated with a solution of 2 : 4-dinitrophenylhydrazine (see above), and the orange oil formed was extracted with benzene and chromatographed to yield **4 : 4-dimethylpentan-2-one** 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 100°.

Attempted Hydration of **3 : 3-Dimethylpent-4-yn-2-one** *and* **2 : 2 : 5 : 5-Tetramethylhept-6-yn-4-one**.—The acetylenic ketone (0·05 mole) was added dropwise during 30 min. to well-stirred boiling solution of mercuric oxide (0·25 g.) in 10% dilute sulphuric acid. After a further hour's heating and stirring the mixture was steam-distilled. Distillation of the dried ($MgSO_4$) and washed (water) ethereal extract of the distillate gave only unchanged acetylenic ketone. The same result was obtained when the amount of mercuric oxide was increased, the reaction time extended (10 hr.), or the solution made homogeneous with ethanol.

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Oxidation of Organic Sulphides. Part III. A Survey of the Autoxidizability of Monosulphides.*

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The reactivity of a variety of organic monosulphides towards molecular oxygen has been investigated at temperatures from 45° to 75°. Formally saturated sulphides by themselves are inert, allylic acyclic sulphides react initially much faster than comparable unsaturated hydrocarbons, and allylic and vinylic cyclic sulphides are still more reactive. Oxygen absorption is promoted by light, by the free-radical catalyst αα′-azo*iso*butyronitrile, and by certain metallic compounds, but not by peroxides. The azo-compound is sufficiently active to catalyse the oxidation of saturated sulphides having C–H bonds adjacent to the sulphur atom, while aryl alkyl sulphides also respond to photo-catalysis.

A notable feature of these autoxidations is the self-inhibition or strong retardation which generally becomes apparent at small oxygen uptakes.

Certain mechanistic details which can be deduced from the experimental findings are discussed.

The reactivity of organic sulphides towards molecular oxygen has not hitherto been investigated despite its relevance to important industrial problems. Chief amongst these is the oxidative ageing of ordinary (sulphur-cured) rubber vulcanisates, and here the omission has been partly deliberate in the sense that a rational approach has only become possible with recent advances in the understanding of the mode of sulphur combinations (see Bateman, Glazebrook, Moore, and Saville, Proc. Third Internat. Rubber Tech. Conf., London, 1954, in the press).

This paper reports a survey of autoxidizability of a number of saturated and unsaturated, cyclic and acyclic, monosulphides. We propose later to consider the influence of multi-sulphur linkages, the nature of the oxidation products, and the olefin–sulphide co-oxidation system which a sulphur vulcanisate exemplifies.

Experimental

Alkyl- and Phenyl-substituted Sulphides.—Dibutyl, dibenzyl, and diphenyl sulphides were commercial specimens purified by conventional methods. Benzyl *n*-propyl, methyl 1-phenylethyl, and diphenylmethyl methyl sulphides were synthesized by standard methods. *n*-Butyl methyl and *cyclo*hexyl methyl sulphides and 2-ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane were kindly provided by Mr. J. Ford, Dr. D. Barnard, and Mr. R. W. Glazebrook, respectively. The purified sulphides (see below) were characterized physically as shown in Table 1; their purity was checked by analysis in all cases, but these data are given for the new compounds only.

Table 1.

	B. p./mm.	n_D^{20}	C (%) Found	C (%) Reqd.	H (%) Found	H (%) Reqd.	S (%) Found	S (%) Reqd.
Bu^n·SMe	122·5°/760	1·4475	—	—	—	—	—	—
Bu^n·SBu^n	71°/14	1·4525	—	—	—	—	—	—
cyclo-C_6H_{11}·SMe	62·5°/13	1·4945	—	—	—	—	—	—
CH_2·CEtMe / CH_2–CHPr^i S (I)	87°/10	1·4760	—	—	—	—	—	—
Ph·SPh	95°/0·02	1·6320	—	—	—	—	—	—
Ph·CH_2·SPr^n	110°/12	1·5429	72·2	72·2	8·5	8·5	19·5	19·6
Ph·CH_2·S·CH_2Ph	(M. p. 49·5°)	—	—	—	—	—	—	—
Ph·CHMe·SMe	89°/12	1·5510	71·1	71·1	8·0	7·9	21·1	21·0
Ph_2CH·SMe	(M. p. 33°)	—	78·6	78·5	6·7	6·6	15·0	15·0

* Part II, *Proc. Roy. Soc.*, 1954, *A*, **224**, 399.

Allylic Acyclic Sulphides.—These were prepared by treatment of the corresponding allylic chloride or bromide with the sodium salt of the appropriate thiol in alcohol. Where necessary the chlorides were subjected to high-efficiency fractionation to ensure isomeric homogeneity (tested by infra-red spectroscopy). Conditions of halide replacement were chosen to ensure direct (S_N2) substitution. No difficulty was experienced with concomitant alcoholysis. The sulphides were washed with water and then fractionated through high-efficiency columns, and contained no detectable amounts of possible isomers as revealed by their infra-red spectra. Their preparation by reaction of a halide with a suspension of the sodium salt of a thiol in benzene or toluene is to be avoided as the sulphide–hydrocarbon azeotropes often obtained on subsequent fractionation are difficult to separate.

The *cyclo*hexenyl and cinnamyl sulphides were kindly provided by Dr. F. W. Shipley (see following paper) and Dr. D. Barnard, respectively.

Physical properties and analyses are recorded in Table 2.

TABLE 2.

	B. p./mm.	n_D^{20}	C (%) Found	C (%) Reqd.	H (%) Found	H (%) Reqd.	S (%) Found	S (%) Reqd.
CH_2:CH·CH_2·SBu^n	73°/14	1·4677	—	—	—	—	—	—
$(CH_2$:CH·$CH_2)_2$S	33°/16	1·4905	—	—	—	—	—	—
CH_2:CH·CHMe·SBu^n ...	61°/15	1·4655	—	—	—	—	—	—
CHMe:CH·CH_2·SMe ...	126°/760	1·4780	58·9	58·8	9·9	9·9	31·1	31·3
CHMe:CH·CH_2·SBu^n ...	72°/14	1·4742	—	—	—	—	—	—
CHMe:CH·CH_2·SPh ...	50°/0·1	1·5695	—	—	—	—	—	—
CHMe:CH·CHMe·SMe	138°/749	1·4707	62·0	62·0	10·4	10·4	27·6	27·6
CHMe:CH·CHMe·SPr^n	60°/13	1·4688	66·4	66·6	11·2	11·1	22·3	22·3
CHMe:CH·CHMe·SPr^i	55°/17	1·4650	66·4	66·6	11·2	11·1	22·2	22·3
CHMe:CH·CHMe·SBu^n	81°/15	1·4688	68·2	68·3	11·5	11·4	20·1	20·3
CHMe:CH·CHMe·SBu^t	66·5°/13	1·4666	68·1	68·3	11·3	11·4	20·2	20·3
CHMe:CH·CHMe·SPh	118°/14	1·5542	73·9	74·1	7·9	7·9	18·1	18·0
R = R·SMe	64·5°/14	1·5210	—	—	—	—	—	—
R·SEt	76°/14	1·5140	—	—	—	—	—	—
R·SPr^i	84°/14	1·5062	—	—	—	—	—	—
R·SBu^t	97°/14	1·5015	—	—	—	—	—	—
R·SPh	82°/0·005	1·5929	—	—	—	—	—	—
CHPh:CH·CH_2·SBu^n ...	100°/0·05	1·5660	—	—	—	—	—	—
CHPh:CH·CH_2·SPh ...	(M. p. 77—78°)	—	—	—	—	—	—	—

Unsaturated Cyclic Sulphides.—The unsubstituted thia*cyclo*hexenes were prepared by Mr. J. Ford according to published procedures; the synthesis of the remaining examples will be described elsewhere (Bateman and Glazebrook, forthcoming publication): see Table 3.

TABLE 3.

	B. p./mm.	n_D^{20}		B. p./mm.	n_D^{20}
(II)	142·5°/758	1·5330	(IV)	66°/10	1·5280
(III)	36°/12	1·5346	(V)	64°/10	1·4932
	50°/10	1·5258			

Treatment of Sulphides with Alumina.—Immediately before use, the neat sulphides were run through alumina contained in a silica tube under an atmosphere of oxygen-free nitrogen. The treatment eliminated variable induction periods and minor variations in oxidation rates.

Other Materials.—*n*-Butyl cinnamyl sulphoxide, prepared and purified as described by Barnard and Hargrave (*Analyt. Chim. Acta*, 1951, **5**, 536), had m. p. 66°. Cinnamaldehyde (n_D^{20} 1·6195) and dibutyl disulphide (n_D^{20} 1·4934) were commercial samples purified by fractionation. 4-Ethylthiobutan-2-one (n_D^{20} 1·4724) and 3-ethylthiobutanal (n_D^{20} 1·4750) were prepared by addition of ethanethiol to methyl vinyl ketone and crotonaldehyde, respectively.

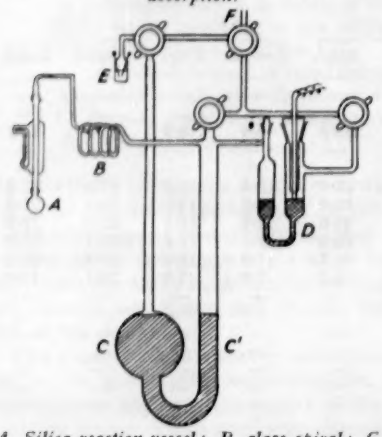
Commercial specimens of quinol (m. p. 170·5°), 2 : 6-di-*tert.*-butyl-*p*-cresol (OH = 1) (m. p. 69·5—70·5°), α-naphthol (m. p. 94·5°), and phenyl-β-naphthylamine (m. p. 107·5°) were recrystallized to constant m. p. αα′-Azo*iso*butyronitrile was purified by successive precipitations from

chloroform solutions with light petroleum. Benzoyl peroxide was purified first by crystallization from ether and then by precipitations from chloroform solution with methanol. *tert.*-Butyl and *cyclo*hex-2-enyl hydroperoxides were of the purity described by Barnard and Hargrave (*ibid.*, p. 479).

Cobalt stearate was purchased from Messrs. Boake Roberts Ltd. and was used directly. The iron and copper phthalocyanines were highly purified samples, kindly supplied by Professor R. P. Linstead.

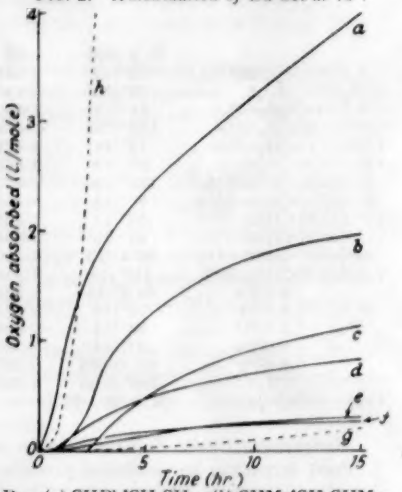
Oxidation Procedure.—A constant-pressure type of apparatus was employed as shown in Fig. 1. As certain of the cyclic sulphides and those containing the 1 : 3-dimethylallyl group showed a sensitivity to the nature of the containing vessel and possibly also to mercury vapour, all the measurements now reported were made by using a transparent silica reaction vessel and an involatile silicone as the manometric fluid.

FIG. 1. *Apparatus for measuring oxygen absorption.*



A, Silica reaction vessel; B, glass spiral; C, burette with silicone fluid; D, pressure-control device with sodium nitrite in trimethylene glycol as conducting fluid; E, gas generator for pressure equalization; F, outlet to pumps and oxygen supply. A was immersed in a thermostat at the required temperature, the remainder of the apparatus in a tank at 25·00° ± 0·05°. Rise in limb C' measured by cathetometer.

FIG. 2. *Autoxidation of* Bu^{n}SR *at 75°.*



R = (*a*) CHPh:CH·CH$_2$·, (*b*) CHMe:CH·CHMe·, (*c*) CH$_2$:CH·CHMe·, (*d*) CHMe:CH·CH$_2$·, (*f*) CH$_2$:CH·CH$_2$·. *Curves* (*e*), (*g*), *and* (*h*) *refer to diallyl sulphide, methyl oleate, and ethyl linoleate respectively.*

Sulphoxide Estimations.—The oxidized mixtures were analysed for sulphoxide by Barnard and Hargrave's titanous chloride method (*loc. cit.*).

Peroxide Estimations.—The formation of hydroperoxides in the autoxidizing sulphide was tested by the sensitive ferrous thiocyanate method (Bolland, Sundralingam, Sutton, and Tristram, *Trans. Inst. Rubber Ind.*, **1941**, **17**, 29) and was found to be too small for accurate estimation.

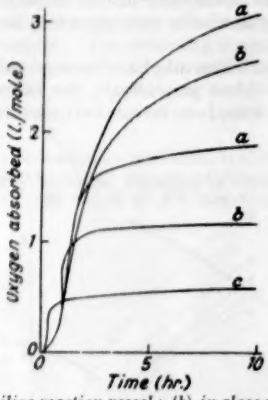
The disappearance of hydroperoxides added to the sulphides as potential catalysts was followed by the stannous chloride method (Barnard and Hargrave, *loc. cit.*)

RESULTS

General Characteristics.—Most unsaturated sulphides react readily with oxygen at 75°—much more readily initially than a comparable mono-olefin, and somewhat similarly to a 1 : 4-diolefin (see Fig. 2). In contrast to behaviour with olefins, however, a marked retardation develops at an early stage in the reaction, and oxygen absorption often ceases when only a small fraction of a mole of oxygen has been absorbed. Such intense autoinhibition appears to be unique for autoxidations, although a milder form is not uncommon and is associated with the

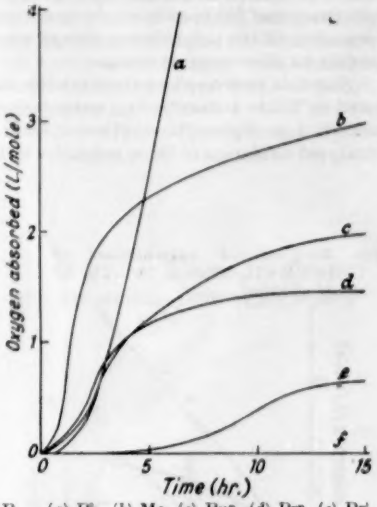
formation of inhibitory substances as a result of decomposition of the primary product. Two processes therefore contribute to the overall oxidation picture: the first, predominating in the earlier stages, is the interaction between the substrate and oxygen; the second, of increasing importance as reaction proceeds, is the interference caused by the secondary reaction products.

FIG. 3. *Autoxidation of* CHMe:CH·CHMe·SMe *at 75°.*



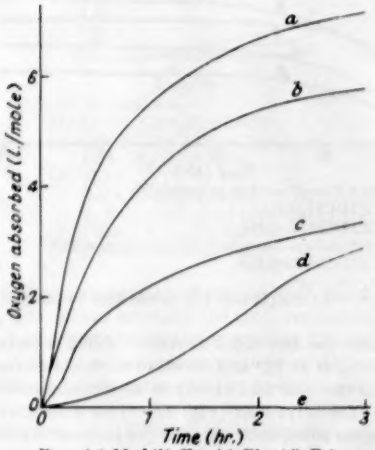
(*a*) *In silica reaction vessel*; (*b*) *in glass reaction vessel*; (*c*) *in the presence of powdered glass.*

FIG. 4. *Autoxidation of* CHMe:CH·CHMe·SR *at 75°.*



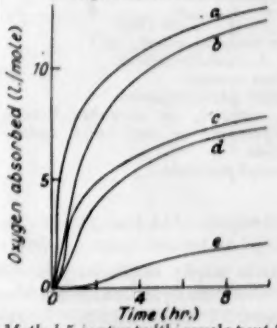
R = (*a*) Ph, (*b*) Me, (*c*) Bu^n, (*d*) Pr^n, (*e*) Pr^i, (*f*) Bu^t (*no uptake*).

FIG. 5. *Autoxidation of* cycloC_6H_9SR *at 75°.*



R = (*a*) Me, (*b*) Et, (*c*) Ph, (*d*) Pr^i, (*e*) Bu^t (*no uptake*).

FIG. 6. *Autoxidation of unsaturated cyclic sulphides at 55°.*



(*a*) 2-*Methyl*-5-*isopropylthia*cyclo*pent*-2-*ene*.
(*b*) 2-*Methylthia*cyclo*hex*-2-*ene*.
(*c*) *Thia*cyclo*hex*-2-*ene*.
(*d*) *Thia*cyclo*hex*-3-*ene*.
(*e*) 2 : 3-*Dimethylthia*cyclo*hex*-2-*ene*.

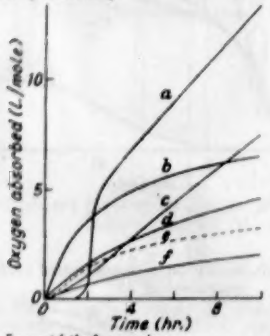
Only brief reference will be made to the latter here since its detailed consideration requires full product analysis (to be reported later); our present concern is mainly with the response of the primary reaction to structural changes and to catalysts and inhibitors.

Reproducibility.—Care being given to synthesis and purification and to the pre-treatment with alumina immediately before use, no trouble was experienced with most of the sulphides in obtaining reproducible rates and extents of oxygen absorption. A few cases presented difficulties, however, which are illustrated for the worst example (1 : 3-dimethylallyl methyl sulphide)

in Fig. 3. In Pyrex vessels, large variations in the total absorptions were observed, with comparatively minor differences in the initial rates of absorption. The use of silica vessels led to a more reproducible but essentially the same initial rate, and reduced, but did not eliminate, the variability in uptake. The addition of powdered glass had a more profound effect, the initial rate being considerably increased and the total uptake being reduced. The glass presumably catalyses the decomposition of a primary product so that inhibitors are formed at an earlier stage than otherwise. 1 : 3-Dimethylallyl *n*-propyl sulphide, but-2-enyl methyl sulphide, and thia-*cyclo*hex-2-ene behaved similarly but to a lesser degree; the sensitivity in this respect of the remainder of the sulphides examined was very small. All the results now reported, however, pertain to silica reaction vessels.

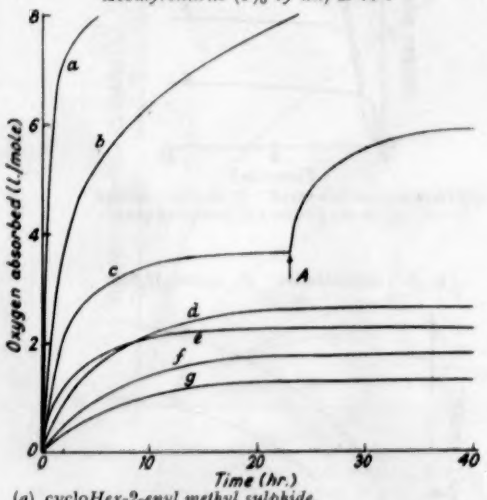
Sulphide Structure and Oxidizability.—Saturated sulphides. The alkyl and phenyl sulphides listed in Table 1 absorbed no oxygen during 24 hr. at 75°. More surprisingly (see below), the benzyl- and diphenylmethyl-substituted compounds were found to be similarly inert. The catalysed oxidation of these sulphides is discussed below.

FIG. 7. *Catalysed autoxidations of* $CHPh{:}CH{\cdot}CH_2{\cdot}SBu^n$ *at* 75° (1% *by wt. of additive*).



(*a*) *Iron phthalocyanine.*
(*b*) *αα'-Azoisobutyronitrile.*
(*c*) *Cobalt stearate.*
(*d*) *Copper phthalocyanine.*
(*e*) *No catalyst, or* cyclo*hex-2-enyl hydroperoxide or* tert.*-butyl hydroperoxide.*
(*f*) *Benzoyl peroxide.*

FIG. 8. *Autoxidation of sulphides catalysed by αα'-azoisobutyronitrile* (1% *by wt.*) *at* 75°.



(*a*) cyclo*Hex-2-enyl methyl sulphide.*
(*b*) $CHPh{:}CH{\cdot}CH_2{\cdot}SBu^n$.
(*c*) $CHMe{:}CH{\cdot}CHMe{\cdot}SMe$.
(*d*) *2-Ethyl-2-methyl-5-isopropylthia*cyclo*pentane.*
(*e*) $CHMe{:}CH{\cdot}CHMe{\cdot}SBu^t$.
(*f*) $Ph{\cdot}CH_2{\cdot}S{\cdot}CH_2Ph$.
(*g*) $MeSBu^n$. *At A a further* 1% *of catalyst was added.*

Acyclic allylic sulphides. (*a*) Effect of substitution on the allyl system. Allyl *n*-butyl sulphide and diallyl sulphide react rather slowly with oxygen at 75° and reaction virtually ceases at about 0·3 l./mole (Fig. 2). Marked increases in both the rate and extent of absorption occur on progressive substitution of methyl and phenyl into the allyl unit (Fig. 2). The differences are qualitatively parallel to those associated with analogous substitutional changes in unsaturated hydrocarbons (Bolland, *Trans. Faraday Soc.*, 1950, **46**, 358).

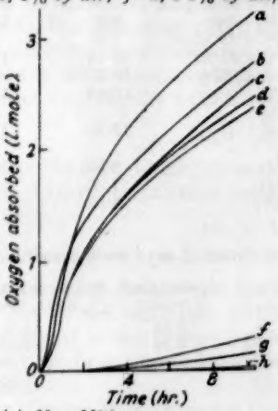
(*b*) Influence of the alkyl substituent in allyl alkyl sulphides. Changes in the saturated or quasi-saturated component in an allyl alkyl sulphide can produce large changes in reactivity, as illustrated for 1 : 3-dimethylallyl and *cyclo*hexenyl compounds in Figs. 4 and 5 respectively. Through the series, methyl, ethyl, *iso*propyl, *tert.*-butyl, the oxidizability decreases progressively until with the last substituent the compounds behave as though they were saturated, *i.e.*, are of negligible reactivity under the experimental conditions. The possibility that the more bulky substituents sterically hinder the approach of reactants to the activated methylene group adjacent to the sulphur atom was shown to be of limited validity by the comparable response of the analogous amethyl and *tert.*-butyl compounds to catalysis by azo*iso*butyronitrile (see Fig. 8).

It thus appears that the decrease in autoxidizability reflects some intrinsic antioxidant activity by the sulphide itself.

Cyclic sulphides. Compared with comparable acyclic compounds, unsaturated cyclic sulphides are oxidized much more rapidly and show less intense auto-inhibition (see Fig. 6, which gives absorption characteristics at 55°, not 75°, as for the acyclic sulphides). This is especially so for a substituted thia*cyclo*pentene with vinylic unsaturation.

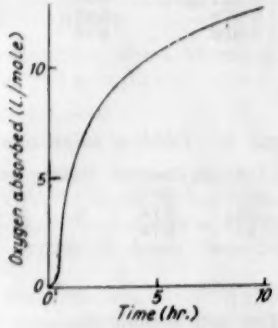
Catalysts and Inhibitors.—Effect of different catalyst types. The oxidation of *n*-butyl cinnamyl sulphide is promoted by a number of common oxidation catalysts (Fig. 7). The important and significant exceptions are benzoyl peroxide, *tert.*-butyl hydroperoxide, and *cyclo*hex-2-enyl hydroperoxide. The following experiments show that the catalytic inactivity of the peroxides cannot be attributed to abnormally rapid destruction in the sulphides. (i) *n*-Butyl cinnamyl sulphide (10 ml.), containing *tert.*-butyl hydroperoxide (0·1034 g.), was heated at 75° in the presence of oxygen. Samples withdrawn at intervals of 1, 2, and 6 hr. after mixing had the following proportions of the original peroxide content present: 46, 28, and 15%, respectively. (ii) The above sulphide (10 ml.), containing benzoyl peroxide (0·5 g.), when heated at 75° for 1 hr. had a peroxide content equal to 10% of the original solution.

FIG. 9. *Autoxidation of* $CHPh{:}CH{\cdot}CH_2{\cdot}SBu^n$ *in the presence of various additives at* 75° (*b—e*, 1% *by wt.*; *f—h*, 0·1% *by wt.*).



(*a*) *No addition.*
(*b*) $CHPh{:}CH{\cdot}CH_2{\cdot}SO{\cdot}Bu^n$.
(*c*) $CHPh{:}CH{\cdot}CHO$ *or* $Bu^n{}_2S_2$ *or* $EtS{\cdot}CH_2{\cdot}CH_2{\cdot}COMe$.
(*d*) H_2O.
(*e*) $EtS{\cdot}CHMe{\cdot}CH_2{\cdot}CHO$.
(*f*) 2 : 6-*Di*-tert.-*butyl*-p-*cresol*.
(*g*) *Phenyl-β-naphthylamine.*
(*h*) *Quinol or α-naphthol.*

FIG. 10. *Autoxidation of* $CHPh{:}CH{\cdot}CH_2{\cdot}SPh$ *at* 75°.



Effect of αα′-azoisobutyronitrile on different sulphide types. As shown in Fig. 8, azo*iso*butyronitrile not only promotes the oxidation of unsaturated sulphides but catalyses the oxidation of otherwise inert saturated types. This is also true of the unsaturated *tert.*-butyl-substituted sulphides, *e.g.*, $CHMe{:}CH{\cdot}CHMe{\cdot}SBu^t$. Diphenyl sulphide, which has no alkyl-type C–H bonds, provides an exception in not responding to such catalysis. The function of the azo-compound as a chain initiator is strikingly shown in example (*c*) (Fig. 8), where a reaction which stops when the added catalyst has wholly decomposed re-starts at almost the same rate on the addition of further catalyst (this has been repeated successively several times).

Photocatalysis. Irradiation with a mercury-vapour lamp through silica or Pyrex glass increases the rate of oxygen uptake and reduces auto-inhibition in those sulphides which autoxidize in the dark. Of those which are inert in the dark (p. 1600), benzyl sulphides, but not dialkyl or diphenyl sulphides, undergo photo-oxidation.

Inhibitors. The common amine and phenolic types of oxidation inhibitor strongly retard the autoxidation of *n*-butyl cinnamyl sulphide (Fig. 9). 4-Ethylthiobutan-2-one, a type of

compound claimed to be an anti-oxidant for unsaturated natural fats (Thompson, *Ind. Eng. Chem.*, 1951, **43**, 1638), and the related 3-ethylthiobutanal exert little effect, as do the major oxidation products of the sulphide, *viz.*, *n*-butyl cinnamyl sulphoxide, cinnamaldehyde, dibutyl disulphide, and water (Barnard, unpublished results; also cf. Bateman and Shipley, *J.*, in the press).

Sulphoxide Formation.—The oxygen uptakes and sulphoxide contents of the various sulphides after reaction with oxygen for 24 hr. under the conditions of the absorption measurements recorded in Figs. 2, 4, 5, 6, and 10, are shown in Table 4. The sulphoxide yields vary with the temperature of oxidation, the trend being illustrated in Table 5.

TABLE 4.

Sulphide	O_2 absorbed (l./mole)	Sulphoxide content (% of absorbed O_2)	Sulphide	O_2 absorbed (l./mole)	Sulphoxide content (% of absorbed O_2)
$CHPh{:}CH{\cdot}CH_2{\cdot}SBu^n$ ...	4·84	23·9	$CHMe{:}CH{\cdot}CH_2{\cdot}SBu^n$ ...	0·78	5·6
$CHMe{:}CH{\cdot}CHMe{\cdot}SBu^n$	2·33	5·0	$(CH_2{:}CH{\cdot}CH_2)_2S$	0·36	11·8
$CH_2{:}CH{\cdot}CHMe{\cdot}SBu^n$ ...	1·40	6·6	$CH_2{:}CH{\cdot}CH_2{\cdot}SBu^n$	0·27	23·0
$CHMe{:}CH{\cdot}CHMe{\cdot}SPh$ ...	6·71	5·7	$CHMe{:}CH{\cdot}CHMe{\cdot}SBu^n$	2·33	5·0
$CHMe{:}CH{\cdot}CHMe{\cdot}SMe$ ...	3·18	5·5	$CHMe{:}CH{\cdot}CHMe{\cdot}SPr^i$	0·78	11·0
$CHMe{:}CH{\cdot}CHMe{\cdot}SPr^n$ ...	1·57	5·0	$CHPh{:}CH{\cdot}CH_2{\cdot}SPh$ ...	15·1	9·8
R = R·SMe	7·94	13·4	(V)	15·93	17·5
R·SEt	6·40	13·2		13·10	15·0
R·SPh	3·93	4·6			
R·SPr^i	3·83	13·2	(II)	8·90	20·2
			(III)	7·85	52·5
			(IV)	4·52	9·4

TABLE 5. *Yields of sulphoxide in autoxidation of* cyclo*hex-2-enyl methyl sulphide.*

Temp.	Time (hr.)	O_2 absorbed (l./mole)	Sulphoxide content (% of O_2 absorbed)	Temp.	Time (hr.)	O_2 absorbed (l./mole)	Sulphoxide content (% of O_2 absorbed)
35°	73	6·14	24·8	75°	28	7·94	13·4
55	23	8·74	21·3	95	5·5	4·44	13·5

DISCUSSION

The free-radical chain character of the autoxidations is clearly revealed by the catalysis by azo*iso*butyronitrile and by light, and the strong retardation by small additions of common oxidation inhibitors. It follows that the remarkable autoretardation and autoinhibition effects must be attributed to specific interference in the chain initiation or propagation steps by one or more of the reaction products. Details of these processes are at present under investigation.

The relative rates of oxidation of a mono-olefin, a 1 : 4-diolefin, and an allylic sulphide (see Fig. 2) suggest that the doubly activated methylene group is the primary reactive centre in the sulphide; cf. $C{:}C{\cdot}CH{\cdot}S$ with $C{:}C{\cdot}\dot{C}H{\cdot}C{:}C$. Critical support for this conclusion is afforded by cinnamyl phenyl sulphide, which is autoxidized very readily (Fig. 10) and possesses only the above type of potentially active C–H bonds. These considerations discount attack by free radicals at the double bond in the allyl unit (in the primary stage), as does other evidence. First, the effect of substitution in the allyl unit (Fig. 2) parallels the relative changes in α-methylenic activity in olefins (Bolland and Gee, *Trans. Farday Soc.*, 1946, **42**, 224; Bolland, *loc. cit.*; Bateman, *Quart. Reviews*, 1954, **8**, 147); secondly, by suitable catalysis, saturated sulphides—with diphenyl sulphide as a significant exception—can be induced to oxidize similarly to their unsaturated counterparts; thirdly, the formation of polymeric products, which would be expected to result if double-bond attack occurred, is inappreciable in allylic sulphides so far examined, but is substantial in the vinylic sulphide, thia*cyclo*hex-2-ene (Ford, unpublished results), where such attack would be expected.

The inhibitory activity of quinol and related substances demonstrates that peroxy- or oxy-free radicals are involved in the propagation step of the autoxidation, and it is therefore reasonable, and consistent with other features such as product composition (Bateman and

Shipley, *loc. cit.*) and substitutional effects, to envisage an autoxidation mechanism comprising the following reactions:

$$CHR{:}CH{\cdot}CH_2{\cdot}SR\ (A) \xrightarrow{(-H)} B \quad (1)$$
$$B + O_2 \longrightarrow BO_2 \quad (2)$$
$$BO_2 + A \longrightarrow BO_2H + B \quad (3)$$
$$BO_2H \longrightarrow BO + OH \quad (4)$$
$$A + OH \longrightarrow B + H_2O \quad (5)$$
$$BO \longrightarrow CHR{:}CH{\cdot}CHO + RS \quad (6)$$
$$2RS \longrightarrow R_2S_2 \quad (7)$$

where B represents the radical $CHR{:}CH{\cdot}\dot{C}H{\cdot}SR$, and BO, BO_2, and BO_2H are the derived radicals and compound. The last would be expected to be highly unstable, of merely transitory existence, decomposing with ease into the aldehyde, water, and disulphide as suggested in reactions (4), (5), (6), and (7).

The formation of sulphoxides as reaction products, sometimes in substantial amount (Table 4), has still to be explained. For this, two supplementary processes are possible. First, since hydroperoxides are known to oxidize sulphides molecularly under conditions comparable with those of autoxidation (Part II, *loc. cit.*), the unstable compound (BO_2H) may react very rapidly with the substrate according to:

$$BO_2H + A \longrightarrow BOH + CHR{:}CH{\cdot}CH_2{\cdot}SOR \quad (8)$$

Secondly, the peroxy-radicals may oxidize the combined sulphur atoms, liberating the oxy-radicals (BO) which can then react as in reaction (10) as well as in (6):

$$BO_2 + A \longrightarrow BO + CHR{:}CH{\cdot}CH_2{\cdot}SOR \quad (9)$$
$$BO + A \longrightarrow BOH + B \quad (10)$$

Common to both possibilities is that the hemithioacetal (BOH), rather than BO_2H, is the precursor of the oxidation scission products (see above), which is not unreasonable having regard to our meagre knowledge of hemithioacetals (Levi, *Gazzetta*, 1932, **62**, 775; Schubert, *J. Biol. Chem.*, 1936, **114**, 341; Kipnis and Ornfelt, *J. Amer. Chem. Soc.*, 1952, **74**, 1068).

The significant mechanistic feature introduced by reactions (9) and (10) is the designation of the oxy-radical (BO) as the dehydrogenating chain carrier, and this may well be responsible for certain special characteristics of sulphide autoxidation which are at present difficult to explain. Thus, just as the greater oxidizability of aldehydes compared with olefins seems to reflect the greater reactivity of acylperoxy- compared with alkenylperoxy-radicals (Bateman and Morris, *Trans. Faraday Soc.*, 1953, **49**, 1026), so the ease of oxidation of unsaturated sulphides may reflect mainly the high reactivity of BO radicals in reaction (10). This in turn is undoubtedly connected with the surprising lack of catalytic activity by peroxides despite the normal behaviour of azo*iso*butyronitrile. It has been shown that this difference cannot be attributed to rapid destruction of the peroxides in the reaction system, and appears to be explicable only in terms of highly specific reactivity of the radicals derived from the various additives. The inactivity of benzoyl peroxide, which is so generally a free-radical catalyst, is puzzling but not unique, for it fails to promote the decarbonylation of aldehydes whereas alkoxy-radicals are effective (Waters, *Nature*, 1952, **170**, 212).

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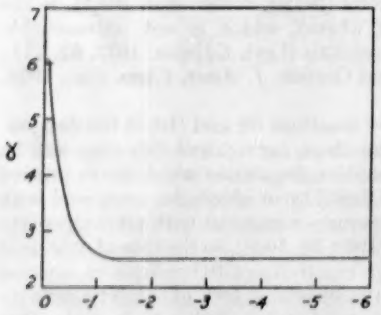
The Purification of Germanium: The Germanium Tetrachloride–Arsenic Trichloride System.

By Mino Green and James A. Kafalas.

[Reprint Order No. 5943.]

The vapour–liquid equilibrium has been determined over a wide concentration range in the anhydrous system: germanium tetrachloride–arsenic trichloride. A relative volatility of 2·52 ± 0·035 was found for mixtures containing less than 0·05 mole fraction of arsenic trichloride in the liquid. Distillation in a Pyrex glass assembly or a quartz assembly gave theoretically predicted values of fractionation if the arsenic concentration was followed with radioactive ^{74}As. However, if the arsenic fractionation was determined by absolute arsenic analysis the Pyrex assembly gave very low fractionation whereas the quartz assembly gave nearly ideal values. This discrepancy for a Pyrex distillation unit is attributed to the leaching of arsenic from the glassware. Germanium tetrachloride containing less than $6{\cdot}30 \times 10^{-10}$ mole fraction of arsenic trichloride was obtained by distillation in a quartz apparatus.

The purification of germanium tetrachloride has attracted attention because of its importance in the preparation of pure germanium (Thompson and Musgrave, *J. Metals*, 1952, **4**, 3). The anhydrous system germanium tetrachloride–arsenic trichloride has been investigated by Sebba (*J.*, 1951, 1975), who found that the vapour–liquid equilibrium curve showed no azeotropes and so concluded that the two compounds could be separated by fractional distillation. The system was also studied in a packed fractionating column by Cluley and Chirnside (*J.*, 1952, 2275). They reported high overall separation when the mole fraction of arsenic trichloride was 10^{-5} or greater, but comment that "when the starting material contained only a few parts per million of arsenic the purification factor achieved was very small and this work showed that redistillation was of little value." The present investigation was undertaken to test the practicability of fractional distillation as a method for obtaining pure germanium tetrachloride (*i.e.*, $[AsCl_3]/[GeCl_4] < 10^{-8}$), and, if possible, to explain the results obtained by Cluley and Chirnside. In particular it seemed difficult to understand the rapid decrease in fractionation at low concentrations of arsenic trichloride.



Variation of relative volatility with composition.

The re-examination of the $GeCl_4$–$AsCl_3$ vapour–liquid system has given results in substantial agreement with Sebba's data. In addition, a more detailed study of the system in the region poor in arsenic trichloride shows that the relative volatility is constant from 5×10^{-2} mole fraction of arsenic trichloride in the liquid down to 6×10^{-10}. This is not surprising since every arsenic trichloride molecule must be entirely surrounded by germanium tetrachloride molecules and so mutual interactions between arsenic trichloride molecules are negligible. In the part of the system which is poor in germanium tetrachloride the same reasoning applies and the relative volatility becomes constant at about 5×10^{-2} mole fraction of the latter. This is not obvious from the Figure because of the use of a logarithmic scale for mole fractions. There was no evidence of azeotrope formation.

Distillation showed that the $GeCl_4$–$AsCl_3$ mixtures behaved perfectly normally if concentration changes were followed by a radiotracer method, but the results of absolute arsenic analyses indicate that there is a source of arsenic in the closed distillation assembly. Since an increase in arsenic concentration was detected in a Pyrex distillation assembly but not in a quartz assembly it was concluded that the additional arsenic was obtained by

the leaching action of germanium tetrachloride on the glass. To confirm this hypothesis, germanium tetrachloride of high purity was refluxed in a Soxhlet extractor and the material re-analysed, whereupon an increase in the concentration of arsenic trichloride was detected. The level of contamination with the latter as a result of exposure to Pyrex glass was not always the same as would be expected since the amount of leachable arsenic might well be related to the history of the glassware—*e.g.*, how much previous leaching had occurred or how the glass had been treated, such as the extent of fire polishing or whether it had been cleaned with detergents or dilute hydrofluoric acid. The temperature at which exposure of germanium tetrachloride to Pyrex glass occurred also appears to be important. The species of arsenic leached from the glass is not known. These studies would help to explain Cluley and Chirnside's results.

Finally, it may be said that germanium tetrachloride can be obtained extremely pure if a quartz distillation column is used. The relative volatility is sufficiently large for a column of a small number of plates at total reflux to be used at large take-off rates to give a product sufficiently pure for the making of germanium semiconductors (see Table 2).

Experimental

The experimental work involved the measurement of ratios of concentrations of arsenic trichloride and germanium tetrachloride in the boiler liquid and the vapour condensate of an equilibrium still, and in the still-pot and still-head of a fractionating column.

Materials.—Germanium tetrachloride was obtained commercially (Eagle–Picher Co., Joplin, Mo.); it contained about 0·5 μg. of arsenic per ml. C.P. arsenic trichloride was used.

Arsenic-74 (17·5 days) was used as a tracer in some of the experiments: it was prepared by bombarding germanium with 16-Mev deutrons in the M.I.T. cyclotron. Other radionuclides were formed, but these were short-lived compared with ^{74}As. The only long-lived species was ^{73}As but its radiations were not detectable with the counting arrangement used. The germanium target was processed four weeks after irradiation when essentially all the activity was due to ^{74}As. The target was burned in chlorine in a closed system from which the germanium tetrachloride formed was distilled and carried away about 30% of the arsenic activity available; this amounted to about 1 mc. A superior method for isolating ^{74}As from arsenic-containing germanium samples (90% arsenic recovery) has been developed since this work was completed (Green and Kafalas, *J. Chem. Phys.*, 1954, **22**, 760). Only tervalent arsenic is volatile and so we have the radioactive arsenic as the trichloride.

Estimation of Arsenic Concentrations.—Tracer ^{74}As was used for measuring ratios of arsenic concentrations: only in cases where the specific activity of the starting material was known could the absolute arsenic concentration be determined. The term "specific activity" is used here to mean the ratio of the inactive arsenic concentration to the counting rate, for 1 ml. of solution under certain fixed, arbitrary, conditions. A measure of the arsenic activity was obtained by using a scintillation counter arrangement. A thallium-activated, cylindrical sodium iodide crystal with a coaxial cylindrical hole extending two-thirds of the way into the crystal was used to detect the radiation from ^{74}As.

Absolute arsenic concentrations, in the very low concentration range, were determined by the method of neutron-activation analysis (Smales and Pate, *Analyt. Chem.*, 1952, **24**, 717). The lower limit of arsenic detection was $6·3 \times 10^{-10}$ mole fraction of $AsCl_3$ (Leddicotte, personal communication). Higher arsenic concentrations were determined by the following standard procedure. 1 ml. of the mixture was transferred from a pipette into a weighing bottle and the sample weighed. The mixture was then placed in a dilute solution of sodium hydroxide and finally neutralized with sodium hydrogen carbonate. The weight of arsenic present was determined by titration against a standard iodine solution.

Vapour–Liquid Equilibrium.—The vapour–liquid equilibrium still used was a version of Gillespie's (*Ind. Eng. Chem. Anal.*, 1946, **18**, 575) slightly modified by replacing the usual straight-bore stopcocks with oblique-bore stopcocks having a liquid seal cup, which was filled with mercury. Both germanium and arsenic chlorides react with mercury, the latter reacting more rapidly, but the area of mercury exposed to the binary mixture was very small and so no significant amount of chemical reaction occurred. This was necessary since no stopcock grease was available which was inert to both chlorides. The apparatus was dried thoroughly before charging it with the mixture to avoid hydrolysis.

Mixtures containing a known amount of $^{74}AsCl_3$ were distilled into the apparatus. After equilibrium was reached (in about 1½ hr.), 1-ml. samples of the boiler liquid and the vapour

condensate were drawn off. In the range from 0·09 mole fraction of arsenic trichloride in the starting material to the maximum arsenic trichloride concentration used, the mole fraction was determined by iodine titration. The values obtained were checked by comparing the ^{74}As activity for a 1-ml. sample of solution against the ^{74}As activity of 1 ml. of the starting material, whose specific activity was known. For lower arsenic concentrations the solutions were assayed by comparing ratios of arsenic activities.

The vapour–liquid equilibrium still was not kept at a fixed pressure since it was unnecessary to obtain extremely precise equilibrium values. We required to know the value of the relative volatility, α, for low concentrations of arsenic trichloride in order to study the behaviour of germanium tetrachloride–arsenic trichloride mixtures in a fractionating column, but it was not possible to calculate reliable values of α from Sebba's work (*J.*, 1951, 1975). The average pressure was 762 mm. (max. 772; min. 749 mm.). Since pressure variations were small, the values for boiling temperatures of the mixtures were corrected by use of the approximate Clapeyron equation. The results obtained are summarized in Table 1.

TABLE 1. *Results of vapour–liquid equilibrium measurements.*

	$10^3 \times$ Mole Fraction of $AsCl_3$				$10^3 \times$ Mole Fraction of $AsCl_3$		
Temp.	Liquid	Vapour	α *	Temp.	Liquid	Vapour	α *
125·8°	973	856	6·08	85·3°	82·5	33·4	2·60
117·4	914	635	6·11	84·8	60·5	25·1	2·50
111·5	858	514	5·71	84·8	58·1	23·4	2·58
99·9	669	282	5·15	84·1	13·3	5·24	2·56
96·8	575	227	4·61	84·1	11·6	4·76	2·45
93·7	428	161	3·90	83·6	6·05	2·55	2·38
91·8	339	135	3·29	83·6	1·36	0·51	2·67
90·2	280	107	3·24	83·6	0·136	0·054	2·52
87·2	151	56·1	2·99	83·6	0·0096	0·0040	2·40
85·6	98·4	39·3	2·67	83·6	0·0084	0·0032	2·63

* Relative volatility, $\alpha = [GeCl_4]_{vap.} \times [AsCl_3]_{liq.}/\{[AsCl_3]_{vap.} \times [GeCl_4]_{liq.}\}$.

The variation of α with composition is shown in the Figure, from which it can be seen that α is approximately constant for concentrations below 0·05 mole fraction of arsenic trichloride in the liquid; the average value in this range is $2{\cdot}52 \pm 0{\cdot}035$.

Distillation Studies.—The distillation studies were made with very dilute solutions of arsenic trichloride, in which α is essentially invariant with composition. It was possible to use the Fenske equation and similar relations in interpreting the experimental results obtained.

A fractionating assembly was made from Pyrex glass; the column, which was vacuum jacketed, was 60 cm. long and 2·0 cm. in internal diameter, and was packed with ¼-inch diameter Pyrex glass single-turn Fenske helices. A 500-ml. vacuum-jacketed still-pot was used and heating was provided by an internal Pt–10% Rh resistance heater. A still-head as described by Payne and Perrins (*J. Appl. Chem.*, 1952, **2**, 208) was used: it was possible with this vapour-dividing still-head to vary the take-off rate continuously from 1 part in 10 to 1 part in 500.

The germanium tetrachloride–arsenic trichloride system, at very low concentrations of arsenic trichloride ($<10^{-6}$ mole fraction), was studied in this assembly. Germanium chloride containing $^{74}AsCl_3$ was distilled into the still-pot and the column was operated at a boil-up rate of 3·42 moles per hr. at atmospheric pressure. 1-ml. samples were taken from the still-head and still-pot and the arsenic activities measured; it was then possible to calculate the fractionation obtained. The effect of take-off rate on the fractionation is shown in Table 2. It can be seen that the fractionation is not a very sensitive function of the take-off rate, and this is to be expected for systems where α is large. At total reflux the column had a plate equivalence of $10{\cdot}6 \pm 0{\cdot}42$, which corresponded closely to the values obtained by using a methyl*cyclo*hexane–*n*-heptane test mixture. The platage error was calculated by use of the equation $dn/n = -d\alpha/(\alpha \log_e \alpha)$, where n is the number of theoretical plates, and it was assumed that the errors due to assaying were negligible.

TABLE 2.

Take-off rate *	0·0	0·014	0·032	0·087	0·092	0·176	0·214
$10^{-3} \times$ Fractionation †	266	266	246	61	46	20·8	6·87

* Ratio of amount withdrawn to the boil-up rate. † Ratio of $[^{74}As]$ in still-pot to that in still-head.

Measurements of the absolute arsenic concentration were also made, by neutron-activation analysis, and the results are shown in Table 3. In all cases samples were stored in pure quartz

TABLE 3. *Fractionation calculated from absolute and radioactive assay for Pyrex and quartz stills at total reflux.*

Still	Absolute mole fractions of $AsCl_3$ Still-pot	Still-head	Fractionation (Absolute)	Fractionation (^{74}As)
Pyrex	$2{\cdot}98 \times 10^{-7}$	$3{\cdot}08 \times 10^{-9}$	9·7	2×10^4
	$3{\cdot}27 \times 10^{-7}$	$2{\cdot}90 \times 10^{-9}$	11·3	2×10^4
Quartz	$1{\cdot}64 \times 10^{-7}$	$<6{\cdot}30 \times 10^{-10}$	>260	300
	$1{\cdot}64 \times 10^{-7}$	$<6{\cdot}30 \times 10^{-10}$	>260	600

vessels. Owing to the large discrepancy between the values of fractionation obtained in a Pyrex system by the radioactivation method and the radiotracer method, the germanium tetrachloride–arsenic trichloride system was examined in a quartz fractionating assembly.

A vacuum-jacketed pure quartz-glass column (60 cm. long and 2·0 cm. in internal diameter) was packed with Raschig rings (3 mm. long; 3 mm. diameter) made from quartz tubing. The quartz still-head contained a solenoid-operated liquid divider of the tilting-funnel type. The same Pyrex still-pot was used with the same procedure. The boil-up rate was 3·42 moles per hour and the column efficiency, as measured with tracer arsenic, was $7{\cdot}0 \pm 0{\cdot}42$ theoretical plates at total reflux. The average fractionation obtained from this system, as measured with tracer arsenic, was 400. Two pairs of samples were analysed by neutron-activation analysis and the results of the average of each pair are given in Table 3. The arsenic concentration of the still-head samples was lower than the limit of detection possible by neutron-activation analysis; therefore the values in Table 3 of mole fraction of arsenic trichloride in the still-head and absolute fractionation are given as upper and lower limits, respectively.

To confirm the possible existence of leaching of arsenic from Pyrex, the following experiment was carried out. Germanium tetrachloride, previously purified in a quartz column, was refluxed for 24 hr. in a Soxhlet extractor packed with Fenske helices. The germanium tetrachloride was analysed for arsenic and the results showed a marked increase in arsenic concentration (before refluxing $<6{\cdot}3 \times 10^{-10}$ mole fraction; after refluxing $2{\cdot}52 \times 10^{-9}$ mole fraction of $AsCl_3$). This increased arsenic concentration, while being significant, is somewhat lower than the values obtained in the distillation assembly. However, the two systems are not entirely comparable, in particular because the temperature of the liquid in contact with the Fenske helices in the distillation column was 83° while the temperature of the contacting liquid in the extractor was about 40°. Further, we expect the leaching to be somewhat erratic.

We thank Dr. G. W. Leddicotte, Oak Ridge National Laboratory, for supervising the activation analyses, and for his keen interest. This research was supported jointly by the U.S. Army, U.S. Navy, and U.S. Air Force under contract with the Massachusetts Institute of Technology. The authors record their grateful thanks for this support.

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Triterpenoids. Part XXXIV. The Constitution of cyclo*Laudenol.

By J. A. HENRY, D. S. IRVINE, and F. S. SPRING.

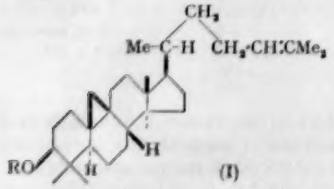
[Reprint Order No. 5954.]

*cyclo*Laudenol, a pentacyclic alcohol obtained from opium, is a C_{31} triterpenoid. Its structure (XXIV) has been elucidated and its stereochemistry defined.

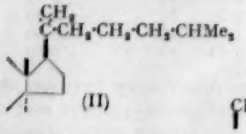
THE isolation of a triterpenoid alcohol, *cyclo*laudenol, from opium was recently described by Bentley, Henry, Irvine, Mukerji, and Spring (*J.*, 1955, 596). *cyclo*Laudenol contains a *cyclo*propane ring and a vinylidene group; the reactions of the dihydro-derivative, *cyclo*laudanol, are very similar to those of *cyclo*artanol. Bentley *et al.* concluded that *cyclo*laudenol and *cyclo*artenol (I; R = H) (Bentley, Henry, Irvine, and Spring, *J.*, 1953, 3673; Barton, Page, and Warnhoff, *J.*, 1954, 2715; Irvine, Henry, and Spring, *J.*, 1955, 1316) have the same nuclear structure and differ only in the nature of the side chain. This

* Part XXXIII, *J.*, 1955, 1316

paper describes experiments which show that this view is correct and that the constitution of *cyclo*laudenol is represented by (XXIV).



(I)



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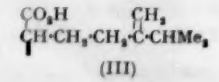

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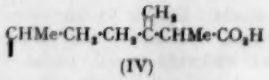

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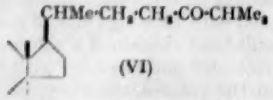

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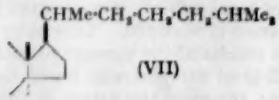

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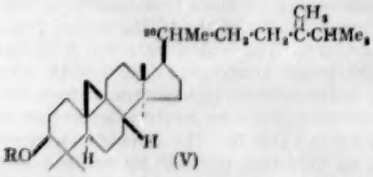


(V)

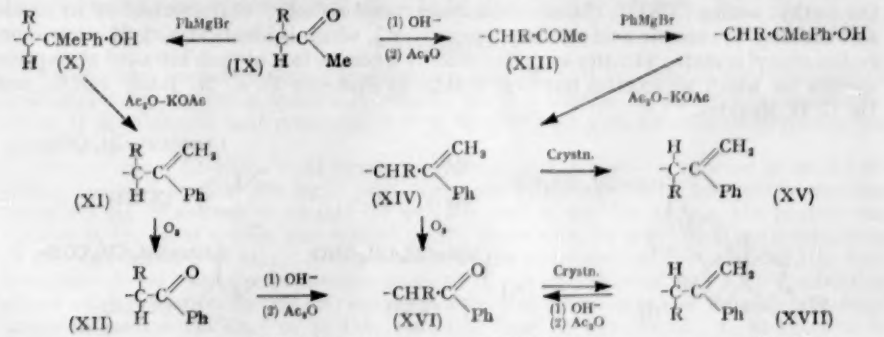
Since *cyclo*laudanol is not identical with *cyclo*artanol, it is unlikely that *cyclo*laudenol differs from *cyclo*artenol simply in the location of the double bond in the side chain. The only structure which would accommodate this view is (II) and this was considered by Bentley *et al.* to be unlikely as it would require that *cyclo*artanol and *cyclo*laudanol differ in configuration around $C_{(20)}$, *i.e.*, that the hydrogenation of the double bond in (II) has proceeded quantitatively to give the unnatural $C_{(20)}$ configuration. The formula (II) for *cyclo*laudenol has been shown to be inadmissible by considerations which emerge below.

Our first approach to the elucidation of the structure of *cyclo*laudenol was to consider the possibility that *cyclo*laudenol is related to a higher homologue of *cyclo*artenol, *i.e.*, that it is a C_{31} or a C_{32} triterpenoid. Eburicoic acid (Holker, Powell, Robertson, Simes, Wright, and Gascoigne, *J.*, 1953, 2422) and the polyporenic acids B and C (Guider, Halsall, Hodges, and Jones, *J.*, 1954, 3234; Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548) are C_{31} triterpenoids of the lanostane group, the C_9 side chains in which have the structure (III); the side chain of the related polyporenic acid A (Halsall and Hodges, *J.*, 1954, 2385; Halsall, Hodges, and Jones, *J.*, 1953, 3019; Roth, Saucy, Anliker, Jeger, and Heusser, *Helv. Chim. Acta*, 1953, **36**, 1908) is represented by (IV). An attractive hypothesis was that *cyclo*laudenol is a C_{31} triterpenoid, and that the double bond has the same position as in the C_{31} triterpenoids named above, *i.e.*, that *cyclo*laudenol is (V; R = H). The latter part of this suggestion was shown to be untenable by the following experiments. Ozonisation of *cyclo*laudenyl acetate yields formaldehyde and a ketone, oxonor*cyclo*laudanyl acetate (Bentley *et al.*, *loc. cit.*, 1955), which we find is reduced, by the Wolff–Kishner method, to nor*cyclo*laudanyl acetate, characterised by its conversion by standard methods into nor*cyclo*laudanol and nor*cyclo*laudanone. If (V; R = Ac) represented *cyclo*laudenyl acetate, oxonor*cyclo*laudanyl acetate would be (VI) and nor*cyclo*laudanyl acetate (VII), *i.e.* nor*cyclo*laudanyl acetate, would be identical with *cyclo*artanyl acetate. However, the last two compounds are distinct, as are the two corresponding alcohols. That nor*cyclo*laudanol differs from *cyclo*artanol simply in configuration round $C_{(3)}$ was considered unlikely because of molecular-rotation considerations and was excluded by the fact that nor*cyclo*laudanone differs from *cyclo*artanone.

We next examined oxonor*cyclo*laudanyl acetate more closely. When treated with potassium hypobromite, this ketone is slowly oxidised to an acid characterised as its methyl ester (methyl 3β-acetoxybisnor*cyclo*laudanoate), thus showing that oxonor*cyclo*laudanyl acetate is a methyl ketone and that the side chain in *cyclo*laudenol is terminated by an *iso*propenyl group. The conversion of *cyclo*laudenyl acetate into oxonor*cyclo*laudanyl acetate and thence into methyl 3β-acetoxybisnor*cyclo*laudanoate is represented as follows: $-CMe{:}CH_2 \longrightarrow -COMe \longrightarrow CO_2Me$. The hypobromite oxidation of the methyl ketone is

very slow, the acid produced is not obtained crystalline, and the ester is isolated in low yield after a tedious purification. Consequently we did not attempt Barbier–Wieland degradation of this ester for elucidation of the nature of the side chain. Instead we attempted to isomerise the side-chain double bond in *cyclo*laudenyl acetate by addition and elimination of hydrogen chloride in the hope that it would be converted into the *iso*propylidene isomer. It was evident that this reaction, even if successful, would be accompanied by fission of the *cyclo*propane ring and formation of a mixture of isomers with nuclear unsaturation but, in spite of this, we hoped that careful ozonolysis of the product would preferentially attack the side-chain double bond. Treatment of *cyclo*laudenyl acetate with dry hydrogen chloride yielded a well-crystalline " hydrochloride " of relatively sharp melting point, undergoing dehydrohalogenation with acetic anhydride to give an acetate, again having a remarkably sharp melting point. Ozonolysis of this gave formaldehyde as the only volatile product. So far as the side chain is concerned the reactions described above have followed the course: $-CHR\cdot CMe{:}CH_2 \rightleftharpoons -CHR\cdot CClMe_2$. An attempt was made to isolate a homogeneous product from the non-volatile fraction of the product obtained from the ozonolysis, but this was unsuccessful, no doubt owing to simultaneous nuclear and side-chain attack by the oxidising agent on the mixture of double-bond isomers resulting from acid fission of the *cyclo*propane ring.

We next turned to a stepwise degradation of oxonor*cyclo*laudanyl acetate. A preliminary examination of this ketone led to a proof that $C_{(24)}$ in *cyclo*laudenol carries an alkyl substituent. Attempts were made to prepare an enol-acetate of oxonor*cyclo*laudanyl acetate to serve as a starting point for side-chain degradations. Using two different methods (see Experimental section) these attempts led instead to a keto-acetate, m. p. 123—125°, $[\alpha]_D$ +52°, different from, and isomeric with oxonor*cyclo*laudanyl acetate, m. p. 140—141°, $[\alpha]_D$ +61°. Hydrolysis of oxonor*cyclo*laudanyl acetate with alkali, followed by reacetylation, gives the same isomer, which is also produced by treatment of the ketone with chromic acid at room temperature. Assuming the designation *b* for the configuration at $C_{(24)}$ in *cyclo*laudenol (and consequently in *oxonorcyclo*laudanyl acetate) (see below), this isomer is named oxonor*cyclo*-24*ab*-laudanyl acetate since, for reasons given in the sequel, we believe it to be a difficulty separable mixture of the 24*a*- and 24*b*-epimers. Reaction of *oxonorcyclo*laudanyl acetate (IX) with phenylmagnesium bromide followed by acetylation yields 25-hydroxy-25-phenylnor*cyclo*laudanyl acetate (X); with acetic anhydride and



		24*b*-Series			24*ab*-Series			24*a*-Series	
		M. p.	$[\alpha]_D$		M. p.	$[\alpha]_D$		M. p.	$[\alpha]_D$
Norketone	(IX)	140—141°	+61°	(XIII)	123—125°	+52°		—	—
Alcohol	(X)	152—154	+37		—	—		—	—
Styryl compound	(XI)	101—102	+56	(XIV)	99—114	+50	(XV)	138—139°	+44°
Phenyl ketone ...	(XII)	112—114	+58	(XVI)	99—102	+49	(XVII)	110—111	+44

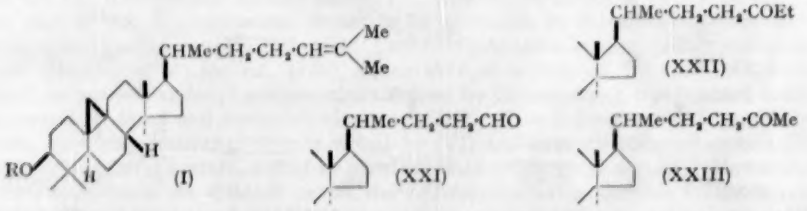
potassium acetate this gives 25-phenylnor*cyclo*laud-25(27)-enyl acetate (XI) which we consider to be the sterically pure 24*b*-epimer. That the dehydration had proceeded in the direction indicated was established by ozonolysis of the styryl compound (XI), formaldehyde (in high yield) and the 24*b*-phenyl ketone (XII) being isolated. The last

compound is also considered to be sterically homogeneous. Similar treatment of oxonor-*cyclo*-24*ab*-laudanyl acetate (XIII) with phenylmagnesium bromide and of the resultant alcohol with acetic anhydride and potassium acetate gives a difficulty separable mixture which we designate 25-phenylnor*cyclo*-24*ab*-laud-25(27)-enyl acetate (XIV). It shows the same ultra-violet absorption spectrum as the 24*b*-isomer (XI). After many crystallisations this gave pure 25-phenylnor*cyclo*-24*a*-laud-25(27)-enyl acetate (XV). Ozonisation of the 24*ab*-styryl compound (XIV) again gave a high yield of formaldehyde together with a ketone considered to be the 24*ab*-phenyl ketone (XVI), the ultra-violet absorption of which was identical with that of the 24*b*-isomer (XII). After many crystallisations this gave the pure 24*a*-phenyl ketone (XVII). Treatment of the 24*a*-phenyl ketone or its 24*b*-isomer with alkali followed by reacetylation gave in each case the 24*ab*-phenyl ketone (XVI) obtained previously from the 24*ab*-methyl ketone (XIII).

Further identification of the 24-alkyl substituent was attempted by treatment of the 24*ab*-phenyl ketone (XVI) with phenylmagnesium bromide. The crude product (XVIII) with acetic anhydride and potassium acetate gave the pure diphenylethylene (XIX) (max. at 2050 and 2430 Å; ε 29,300 and 13,400). Ozonolysis then yielded benzophenone and a ketone (XX) characterised by its oxime.

$$\underset{\text{(XVI)}}{\text{–CHR·COPh}} \longrightarrow \underset{\text{(XVIII)}}{\text{–CHR·CPh}_2\text{·OH}} \longrightarrow \underset{\text{(XIX)}}{\text{–CR:CPh}_2} \longrightarrow \underset{\text{(XX)}}{\text{–COR}}$$

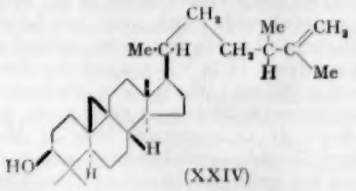
It being established that *cyclo*laudenol and the ketone are related as –CHR·CMe:CH_2 to –COR, identification of R could have been attempted by repetition of the Barbier–Wieland degradation or by conversion of *cyclo*artenol (I; R = H) into 24-oxotrisnor*cyclo*laudanyl acetate, the second method depending on the hypothesis that *cyclo*laudenol and *cyclo*artenol differ solely in the nature of the side chain. Since supplies of *cyclo*laudenol were very limited we examined the second method by reactions chosen, as in the degradation of *cyclo*laudenol, to leave the labile *cyclo*propane bridge intact. Careful treatment of *cyclo*artenyl acetate with ozone gave, in 70% yield, 3β-acetoxytrisnor*cyclo*artan-24-al (XXI), characterised as its dimethyl acetal and oxime. Reaction of the aldehyde (XXI) with diazoethane yielded the ethyl ketone (XXII) (24-oxonor*cyclo*artanyl acetate) characterised by its oxime and by its stability to chromic acid at room temperature; it is different from 24-oxotrisnor*cyclo*laudanyl acetate. The aldehyde was converted by diazomethane into the methyl ketone (XXIII) (24-oxobisnor*cyclo*artanyl acetate; characterised by its oxime and stability to chromic acid at room temperatur), which is identical with 24-oxotrisnor-*cyclo*laudanyl acetate; identity was confirmed by a comparison of their infra-red absorption spectra for which we express our best thanks to Professor E. R. H. Jones, F.R.S., and Dr. G. D. Meakins.



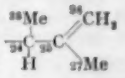
The constitution of *cyclo*laudenol is therefore represented by (XXIV). The one feature of the sterochemistry of *cyclo*laudenol which remains to be defined, namely, the configuration at $C_{(24)}$, was established by molecular-rotation relations. The two possible configurations for the terminal carbon atoms in the side chain of *cyclo*laudenol are represented by (XXV; 24*b* on the current convention) and (XXVI; 24*a*). Bergmann and Low (*J. Org. Chem.*, **1947**, **12**, 67) have shown that the introduction of a 24*a*-methyl group * into cholestanol and cholesterol and their esters causes a substantial positive

* The configurational indices used by Bergmann and Low should be interchanged to conform with presently accepted nomenclature.

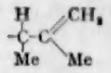
increment (Δ *ca.* +22°) in molecular rotation, whereas a negative change (Δ *ca.* −29°) accompanies the introduction of a 24*b*-methyl group. A comparison of the molecular rotations of lanostane derivatives with those of the corresponding laudane derivatives is



(XXIV)



(XXV)



(XXVI)

shown below; in all cases the Δ value ($[M]_D$ laudane $-[M]_D$ lanostane derivative) is negative, from which we conclude that *cyclo*laudenol is 24*b*-methyl-9 : 19-*cyclo*lanost-25-en-3β-ol (24*b*-methyl*cyclo*art-25-enol) (XXV).

	$[M]_D$		$[M]_D$ [3]	Δ
Lanostane [1]	+145°	Laudane	+107°	−38°
Lanostanol [1]	+150	Laudanol	+ 93	−57
Lanostanyl acetate [1]	+193	Laudanyl acetate	+155	−38
Lanostanone [1]	+116	Laudanone	+ 62	−54
*cyclo*Artanol [2]	+214	*cyclo*Laudanol	+191	−23
*cyclo*Artanyl acetate [2]	+277	*cyclo*Laudanyl acetate	+242	−35
	$[M]_D$ [1]		$[M]_D$ [4]	Δ
Lanost-8-enol	+261°	Eburic-8-enol	+238°	−23°
Lanost-8-enyl acetate	+275	Eburic-8-enyl acetate	+271	− 4
Lanost-8-ene	+272	Eburic-8-ene I	+234	−38
		Eburic-8-ene II	+218	−54

[1] From Elsevier's "Encyclopaedia of Organic Chemistry," Vol. 14S. [2] From Bentley, Henry, Irvine and Spring, *J.*, 1953, 3673. [3] From Bentley, Henry, Irvine, Mukerji and Spring, *J.*, 1955, 596. [4] From Robertson *et al.*, *J.*, 1951, 2346; 1953, 2414.

The Table also includes a comparison of the molecular rotations of lanost-8-enol and eburic-8-enol derivatives. Although the data are more limited than those available in the laudane series, we conclude from the negative value of Δ that eburic-8-enol is 24*b*-methyllanost-8-enol. It follows that the saturated parent of the eburicoic acid group, eburicane (which has not been prepared), will prove to be identical with laudane.

Experimental

Specific rotations were measured in chloroform solution in a 1-dm. tube at room temperature, and ultraviolet absorption spectra in ethanol using a Unicam SP 500 spectrophotometer. Grade II alumina and light petroleum of b. p. 60—80° were used for chromatography unless otherwise specified.

Wolff–Kishner Reduction of 25-Oxo-26-norcyclolaudanyl Acetate.—A mixture of 25-oxo-26-nor*cyclo*laudanyl acetate (250 mg.), 100% hydrazine hydrate (2·5 ml.), and sodium ethoxide (from 312 mg. of sodium) in ethanol (15 ml.) was kept at 200° for 12 hr. The product was isolated in the usual manner and treated on the steam-bath for 3 hr. with acetic anhydride (5 ml.) and pyridine (5 ml.). A dry solution of the acetylated product (236 mg.) in light petroleum (25 ml.) was filtered through a column (1 × 8 cm.) of alumina (6 g.). The fraction eluted with light petroleum (125 ml.) was crystallised from methanol to give 26-*nor*cyclo*laudanyl acetate* as needles (134 mg.), m. p. 118—120°, $[\alpha]_D$ +58° (*c*, 1·1) (Found : C, 81·3; H, 11·6. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%). A mixture with *cyclo*artanyl acetate had m. p. 117—128°. Hydrolysis of the acetate with 3% methanolic potassium hydroxide gave 26-*nor*cyclo*laudanol*, needles (from methanol), m. p. 114—115°, $[\alpha]_D$ +49° (*c*, 1·6) (Found : C, 83·9; H, 12·2. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%). A mixture of 26-nor*cyclo*laudanol and *cyclo*artanol had m. p. 98—110°. Oxidation of 26-nor*cyclo*laudanol with chromic acid in acetic acid for 12 hr. at room temperature and isolation of the product in the usual manner, gave 26-*nor*cyclo*laudan-3-one* which separates from methanol as blades, m. p. 100—101°, depressed to 92—97° when mixed with *cyclo*artanone, $[\alpha]_D$ +22° (*c*, 2·2) (Found : C, 84·0; H, 11·9. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). The *oxime* separates as needles, m. p. 203°, from chloroform–methanol (Found : C, 81·7; H, 11·3. $C_{30}H_{51}ON$ requires C, 81·6; H, 11·6%).

Methyl 3β-*Acetoxy*-26 : 27-*bisnor*cyclo*laudan*-25-*oate*.—25-Oxo-26-nor*cyclo*laudanyl acetate (375 mg.) in dioxan (15 ml.) was shaken with bromine (1 ml.), potassium hydroxide (15 g.), and water (20 ml.) at room temperature for 14 days. The acidic fraction (284 mg.) isolated in the usual manner (insoluble potassium salt) was treated on the steam-bath for 2½ hr. with acetic anhydride (5 ml.) and pyridine (5 ml.). The acetylated acid, which could not be obtained crystalline, was esterified with ethereal diazomethane, and a solution of the methyl ester in light petroleum (25 ml.) was percolated through a column (1·75 × 5 cm.) of alumina (9 g.). Elution with light petroleum–benzene gave a fraction (62 mg.) which, on crystallisation from methanol, yielded *methyl* 3β-*acetoxy*-26 : 27-*bisnor*cyclo*laudan*-25-*oate* as needles, m. p. 115—116°, $[\alpha]_D$ +57° (*c*, 1·1) (Found : C, 76·8; H, 10·5. $C_{32}H_{52}O_4$ requires C, 76·8; H, 10·5%).

Treatment of cyclo*Laudenyl Acetate with Hydrogen Chloride*.—*cyclo*Laudenyl acetate (2 g.) in dry chloroform (40 ml.) was treated with a stream of dry hydrogen chloride at 0° for 3 hr. The solid obtained on removal of the solvent crystallised from methanol, giving a " *hydrochloride* " (1·7 g.) as needles, m. p. 166—170° (decomp.), $[\alpha]_D$ +64° (*c*, 1·3) (Found : C, 76·0; H, 10·8. $C_{32}H_{55}O_2Cl$ requires C, 76·3; H, 10·7%). The compound gives a strong yellow colour with tetranitromethane. A solution of the " hydrochloride " in acetic anhydride (15 ml.) was refluxed for 15 hr., then diluted with water. The product, isolated in the usual manner, separated from chloroform–methanol as needles (1·1 g.), m. p. 152—156°, $[\alpha]_D$ +61° (*c*, 1·1) (Found : C, 81·8; H, 11·0. $C_{32}H_{54}O_2$ requires C, 82·1; H, 11·3%). Ozonised oxygen was then passed through a solution of this product (1·3 g.) in acetic acid (170 ml.) at room temperature for 1 hr. The solution was diluted with water (1 l.), treated with 10% ferrous sulphate solution (20 ml.), and steam-distilled. From the distillate (500 ml.), formaldehyde (22%) was isolated as its dimethone, needles (from ethanol), m. p. and mixed m. p. 190—191° (Found : C, 69·7; H, 8·2. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%). The filtrate from the dimethone derivative was again steam-distilled and the distillate (250 ml.) treated with aqueous 2 : 4-dinitrophenylhydazine hydrochloride; no hydrazone separated. The non-volatile product was treated with chromic acid by the method (Bentley *et al.*, *loc. cit.*, 1953) used for the preparation of laud-9(11)-enyl acetate from the mixture obtained by treatment of *cyclo*laudanyl acetate with hydrogen chloride, but no crystalline product was isolated.

Treatment of 25-*Oxo*-26-*nor*cyclo*laudanyl Acetate with Alkali*.—25-Oxo-26-nor*cyclo*laudanyl acetate (m. p. 140—141°, $[\alpha]_D$ +61°; 200 mg.) was refluxed with 5% methanolic potassium hydroxide (150 ml.) for 5 hr. to yield 25-*oxo*-26-*nor*cyclo-24ab-*laudanol* (138 mg.), separating from aqueous methanol as short, thick needles, m. p. 139—141°, $[\alpha]_D$ +43° (*c*, 1·4) (Found : C, 81·0; H, 11·4. $C_{30}H_{50}O_3$ requires C, 81·4; H, 11·4%). Acetylation of this alcohol (110 mg.) at room temperature for 12 hr. with acetic anhydride (5 ml.) and pyridine (5 ml.) and two crystallisations from methanol gave 25-*oxo*-26-*nor*cyclo-24ab-*laudanyl acetate* as needles (60 mg.), m. p. 123—125° unchanged on further crystallisation, $[\alpha]_D$ +52° (*c*, 1·5) (a mixture with 25-oxo-26-nor*cyclo*laudanyl acetate had m. p. 123—135°) (Found : C, 79·3; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The *oxime* separated from methanol as needles, m. p. 153—154°, $[\alpha]_D$ +50° (*c*, 1·5) (Found : C, 76·6; H, 10·5. $C_{32}H_{53}O_3N$ requires C, 76·9; H, 10·7%). Treatment of 25-oxo-26-nor*cyclo*laudanyl acetate (100 mg.) in acetic acid (25 ml.) with chromic acid (18 mg.) for 12 hr. at room temperature did not give an acidic product. The neutral product furnished 25-oxo-26-nor*cyclo*-24*ab*-laudanyl acetate, separating from methanol as needles (72 mg.), m. p. 123—125° alone or mixed with the specimen described above, $[\alpha]_D$ +53° (*c*, 1·2).

25-Oxo-26-nor*cyclo*-24*ab*-laudanyl acetate was also obtained as follows : (i) A mixture of 25-oxo-26-nor*cyclo*laudanyl acetate (100 mg.), acetic anhydride (2 ml.), and freshly fused potassium acetate (100 mg.) was kept at 132° for 10 hr. The product, isolated in the normal manner, gave 25-oxo-26-nor*cyclo*-24*ab*-laudanyl acetate which, twice crystallised from methanol, gave needles (87 mg.), m. p. 123—125°, $[\alpha]_D$ +51° (*c*, 1·2).

(ii) A solution of the same acetate (100 mg.) in *iso*propenyl acetate (20 ml.) and one drop of concentrated sulphuric acid was kept at 100° for 3 hr. The product was twice crystallised from methanol, to give 25-oxo-26-nor*cyclo*-24*ab*-laudanyl acetate as needles (82 mg.), m. p. 123—125°, $[\alpha]_D$ +52° (*c*, 1·4).

Treatment of 25-*Oxo*-26-*nor*cyclo*laudanyl Acetate with Phenylmagnesium Bromide*.—The acetate (2 g., 1 mol.) in ether (80 ml.) was added during 45 min. to a solution of phenylmagnesium bromide (6 mols.) in ether (100 ml.), and the mixture refluxed for 30 min. The product was steam-distilled for 1 hr. and a solution of the non-volatile fraction (2·4 g.) in acetic anhydride (15 ml.) refluxed with freshly fused potassium acetate (0·5 g.) for 1 hr. A solution of the product in light petroleum (100 ml.) was percolated through a column (2·75 × 15 cm.) of alumina (75 g.), and the fraction (0·6 g.) eluted by light petroleum (900 ml.) crystallised from methanol to give

25-*phenyl*-26-*nor*cyclo*laud*-25(27)-*enyl acetate* as plates, m. p. 101—102°, $[\alpha]_D$ +56° (*c*, 1·2) (Found: C, 83·9; H, 10·4. $C_{38}H_{56}O_2$ requires C, 83·8; H, 10·4%). The styryl compound gives a strong yellow colour with tetranitromethane. Light absorption: max. at 2080 and 2360 Å (ε 12,200 and 8100). The fractions eluted by light petroleum–benzene (1 : 4, 1050 ml.; 1 : 1, 1350 ml.) were combined (1·5 g.) and twice crystallised from acetone–water to give the 25-*hydroxy*-25-*phenyl*-26-*nor*cyclo*laudanyl acetate* as small needles (0·7 g.), m. p. 152—154°, $[\alpha]_D$ +37° (*c*, 1·1) (Found: C, 81·0; H, 10·4. $C_{38}H_{58}O_3$ requires C, 81·1; H, 10·4%). It gives a pale yellow colour with tetranitromethane. Light absorption: max. at 2080 Å (ε 7250). A solution of the alcohol and potassium acetate (0·5 g.) in acetic anhydride (15 ml.) was heated under reflux for 4 hr. and left overnight. The product in light petroleum (80 ml.) was chromatographed on alumina (40 g.), and the fraction eluted by light petroleum (880 ml.) crystallised from methanol to give the styryl compound described above as needles (0·7 g.), m. p. and mixed m. p. 101—102°, $[\alpha]_D$ +55·6° (*c*, 1·1).

Ozonolysis of 25-*Phenyl*-26-*nor*cyclo*laud*-25(27)-*enyl Acetate*.—A solution of the styryl compound (1 g.) in dry chloroform (150 ml.) was treated with ozonised oxygen at −45°. The ozonide was decomposed with zinc and acetic acid, and after filtration the solution was washed with water, and the washings were retained. The product was steam-distilled and a solution of the residue (0·9 g.) in light petroleum (70 ml.) chromatographed on a column (2·25 × 8 cm.) of alumina (30 g.). The fraction (0·5 g.) eluted by light petroleum–benzene (4 : 1, 640 ml.) gave 25-*oxo*-25-*phenyl*-26 : 27-*bisnor*cyclo*laudanyl acetate*, which separates from methanol as needles, m. p. 112—114°, $[\alpha]_D$ +57·5° (*c*, 1·2) (Found: C, 81·1; H, 10·0. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%). The ketone gives a pale yellow colour with tetranitromethane. Light absorption: max. at 2050 and 2420 Å (ε 13,000 and 11,750). The *oxime* separated from methanol as short thick needles, m. p. 177—179°, $[\alpha]_D$ +55° (*c*, 1·3) (Found: C, 78·8; H, 9·7. $C_{37}H_{55}O_3N$ requires C, 79·1; H, 9·9%). From the aqueous washings, formaldehyde was isolated as its dimethone (0·24 g., 44%), needles (from ethanol), m. p. and mixed m. p. 190—191° (Found: C, 69·7; H, 8·4. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%).

Treatment of 25-*Oxo*-26-*nor*cyclo-24ab-*laudanyl Acetate with Phenylmagnesium Bromide*.—25-Oxo-26-nor*cyclo*-24*ab*-laudanyl acetate (3·7 g.) was treated with phenylmagnesium bromide (8·2 g.) as described above. The crude alcohol (4·5 g.) was readily dehydrated by refluxing for 4 hr. with acetic anhydride (30 ml.) and potassium acetate (1 g.). A solution of the product (4·4 g.) in light petroleum (150 ml.) was filtered through a column (4 × 12·5 cm.) of alumina (130 g.). The fractions (2·3 g.) eluted by light petroleum (600 ml.) and light petroleum–benzene (4 : 1, 3 l.) were combined and crystallised from ethanol, from which 25-phenyl-26-nor*cyclo*-24*ab*-laud-25(27)-enyl acetate separated as fine needles (2 g.), m. p. 99—114°, $[\alpha]_D$ +49·8° (*c*, 1·2), which gave a strong yellow colour with tetranitromethane. Light absorption: max. at 2080 and 2360 Å (ε 13,000 and 8700). Nine recrystallisations from ethanol gave 25-*phenyl*-26-*nor*cyclo-24a-*laud*-25(27)-*enyl acetate* as fine needles, m. p. 138—139°, $[\alpha]_D$ +44° (*c*, 1·1) (Found: C, 83·7; H, 10·2. $C_{38}H_{56}O_2$ requires C, 83·8; H, 10·4%).

Ozonolysis of the 24ab-*Styryl Compound*.—Ozonised oxygen (2 mols.) was passed through a solution of the 24*ab*-styryl compound (2 g.; m. p. 99—114°) in dry chloroform (150 ml.) at −45°, and the ozonide treated with zinc and acetic acid. The product (1·9 g.) was isolated by means of chloroform in the usual manner and the washings were retained. After removal of chloroform, the residue was steam-distilled for 1 hr. The non-volatile fraction was dissolved in light petroleum (150 ml.) and filtered through a column (2·75 × 11 cm.) of alumina (60 g.). The fractions (1·1 g.) eluted by light petroleum–benzene (1 : 1, 1800 ml.; 3 : 1, 500 ml.) and benzene (400 ml.) were combined and crystallised from methanol, to yield 25-oxo-25-phenyl-26 : 27-bisnor*cyclo*-24*ab*-laudanyl acetate as needles (0·7 g.), m. p. 99—102°, $[\alpha]_D$ +49° (*c*, 1·4). Light absorption: max. at 2050 and 2420 Å (ε 13,000 and 11,250). Seven crystallisation from methanol gave 25-*oxo*-25-*phenyl*-26 : 27-*bisnor*cyclo-24*a*-*laudanyl acetate*, m. p. 110—111°, $[\alpha]_D$ +44° (*c*, 1·7) (Found: C, 81·1; H, 10·0. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%). A mixture of 25-oxo-25-phenyl-26 : 27-bisnor*cyclo*laudanyl acetate (m. p. 112—114°) and the 24*a*-isomer had m. p. 98—103°, *i.e.* approx. the same as the 24*ab*-mixture described above. From the aqueous washings, formaldehyde (67%) was isolated as its dimethone, needles (from ethanol), m. p. and mixed m. p. 190—191° (Found: C, 69·6; H, 8·0. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%). The filtrate from the dimethone was again distilled and the distillate treated with 2 : 4-dinitrophenylhydrazine; no precipitate was obtained.

Treatment of the 24a- *and* 24b-*Phenyl Ketones with Alkali*.—(i) Hydrolysis of the 24*a*-phenyl ketone (116 mg.) with 3% methanolic potassium hydroxide and treatment of the product with acetic anhydride (5 ml.) and pyridine (5 ml.) at 95° for 1½ hr. yielded the 24*ab*-phenyl ketone

which separated from methanol as needles (84 mg.), $[\alpha]_D$ +47° (*c*, 1·2), m. p. 95—101°, alone or mixed with the specimen of m. p. 99—102°.

(ii) The 24*b*-phenyl ketone (110 mg.) was treated with 5% methanolic potassium hydroxide under reflux for 6 hr. with subsequent reacetylation. Crystallisation from methanol gave the 24*ab*-phenyl ketone (71 mg.), $[\alpha]_D$ +46° (*c*, 1·0), m. p. 96—100° alone or mixed with a specimen of m. p. 99—102°.

25 : 25-*Diphenyl*-26 : 27-*bisnor*cyclo*laud*-24-*enyl Acetate*.—The 24*ab*-phenyl ketone (1·4 g.; m. p. 98—102°) was treated with phenylmagnesium bromide (2·7 g.) as described above. The alcohol was dehydrated (without purification) by refluxing for 4 hr. with acetic anhydride (15 ml.) and potassium acetate. A solution of the product (1·4 g.) in light petroleum (100 ml.) was chromatographed on a column (3 × 8·5 cm.) of alumina (45 g.). The fraction eluted by light petroleum–benzene (4 : 1; 560 ml.) crystallised from chloroform–methanol, from which the *diphenylethylene* separated as plates (0·4 g.), m. p. 170°, $[\alpha]_D$ +53° (*c*, 1·4) (Found : C, 85·0; H, 9·5. $C_{43}H_{58}O_2$ requires C, 85·1; H, 9·6%). It gives a strong yellow colour with tetranitromethane. Light absorption : max. at 2050 and 2430 Å (ε 29,300 and 13,400).

24-*Oxo*-25 : 26 : 27-*trisnor*cyclo*laudanyl Acetate*.—A solution of the diphenylethylene (350 mg.) in dry chloroform (100 ml.) was treated with ozonised oxygen at −45°, and the ozonide treated with zinc and acetic acid. The product (320 mg.) was isolated by means of chloroform in the usual manner and the water-washings were retained. The residue obtained on removal of the solvent was steam-distilled, and a solution of the non-volatile fraction in light petroleum–benzene (1 : 1, 80 ml.) percolated through a column of alumina (1·75 × 6·75 cm., 12 g.). The fraction (77 mg.) eluted by light petroleum–benzene (1 : 3, 250 ml.) crystallised from methanol, to give 24-*oxo*-25 : 26 : 27-*trisnor*cyclo*laudanyl acetate* as plates, m. p. 170°, $[\alpha]_D$ +58° (*c*, 1·2) (Found : C, 78·7; H, 10·8. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). The *oxime* separated from chloroform–methanol as plates, m. p. 219—220°, $[\alpha]_D$ +50° (*c*, 0·8) (Found : C, 76·2; H, 10·2. $C_{30}H_{49}O_3N$ requires C, 76·4; H, 10·5%). Ether-extraction of the aqueous washings gave a clear gum (62 mg.) with a fragrant odour. A solution in methanol (2 ml.) on treatment with Brady's reagent yielded benzophenone 2 : 4-dinitrophenylhydrazone which separated from acetic acid as orange plates (89 mg., 43%), m. p. and mixed m. p. 235—236° (Found : C, 63·1; H, 3·9; N, 15·6. Calc. for $C_{19}H_{14}O_4N_4$: C, 63·0; H, 3·9; N, 15·5%). Light absorption : max. at 2060, 2240, 2500, and 3800 Å (ε 37,800, 26,400, 18,500, and 30,000).

3β-*Acetoxy*-25 : 26 : 27-*trisnor*cyclo*artan*-24-*al*.—Ozonised oxygen (2 mols.) was passed through a solution of *cyclo*artenyl acetate (4 g.) in dry chloroform (200 ml.) at −45°. Treatment of the ozonide with zinc dust and acetic acid and isolation of the product by means of chloroform gave 3β-*acetoxy*-25 : 26 : 27-*trisnor*cyclo*artan*-24-*al*, as prisms (2·8 g.) (from aqueous acetone), m. p. 155—157°, $[\alpha]_D$ +59·5° (*c*, 2·0) (Found : C, 78·7; H, 10·5. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%). From a hot solution of the aldehyde in methanol, 24 : 24-*dimethoxy*-25 : 26 : 27-*trisnor*cyclo*artanyl acetate* separated as prisms, m. p. 125—126°, $[\alpha]_D$ +53° (*c*, 1·1) (Found : C, 76·0; H, 10·7. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%). The *oxime* of the aldehyde separated from methanol as needles, m. p. 198° (Found : C, 75·7; H, 10·1. $C_{29}H_{47}O_3N$ requires C, 76·1; H, 10·3%).

24-*Oxo*-26-*nor*cyclo*artanyl Acetate*.—3β-Acetoxy-25 : 26 : 27-trisnor*cyclo*artan-24-al (2·8 g.) in dry ether (30 ml.) and dioxan (20 ml.) was treated with ethereal diazoethane (50 ml.; from 12 g. of nitrosoethylurea) at room temperature for 2 days. A solution of the product in light petroleum (100 ml.) was filtered through a column (2·5 × 18 cm.) of alumina (90 g.), and the fraction (1·2 g.) eluted by light petroleum–benzene (4 : 1, 1050 ml.; 1 : 1, 1350 ml.) was crystallised from aqueous methanol, to yield 24-*oxo*-26-*nor*cyclo*artanyl acetate* as blades, m. p. 118°, $[\alpha]_D$ +57° (*c*, 1·4) (Found : C, 78·9; H, 10·8. $C_{31}H_{50}O_3$ require C, 79·1; H, 10·7%). The *oxime* separated from methanol as needles, m. p. 160° (Found : C, 77·2; H, 10·4. $C_{31}H_{51}O_3N$ requires C, 76·7; H, 10·6%). The ketone was recovered unchanged after treatment with chromic acid at room temperature.

24-*Oxo*-26 : 27-*bisnor*cyclo*artanyl Acetate*.—3β-Acetoxy-25 : 26 : 27-trisnor*cyclo*artan-24-al (1·4 g.) in dry ether (20 ml.) and dioxan (10 ml.) was treated with ethereal diazomethane (50 ml.; from 5 g. of nitrosomethylurea) at room temperature for 3 days. A solution of the product (1·5 g.) in light petroleum–benzene (4 : 1; 150 ml.) was percolated through a column (2·5 × 17 cm.) of alumina (60 g.). The combined fractions (850 mg.) eluted by light petroleum–benzene (3 : 2, 1200 ml.; 2 : 3, 600 ml.) were crystallised from methanol, to give 24-*oxo*-26 : 27-*bisnor*cyclo*artanyl acetate* as plates, m. p. 170° alone or mixed with 24-oxo-25 : 26 : 27-trisnor*cyclo*laudanyl acetate, $[\alpha]_D$ +58° (*c*, 1·2) (Found : C, 78·9; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; 10·6%). The *oxime* of 24-oxo-26 : 27-bisnor*cyclo*artanyl acetate separated from chloroform–

methanol as needles, m. p. 219—220°, alone or mixed with the oxime of 24-oxo-25 : 26 : 27-trisnor-*cyclo*laudanyl acetate, $[\alpha]_D$ +50° (*c*, 0·9) (Found : C, 76·2; H, 10·0. $C_{30}H_{49}O_3N$ requires C, 76·4; H, 10·5%). 24-Oxo-26 : 27-bisnor*cyclo*artanyl acetate was recovered unchanged after treatment with chromic acid at room temperature.

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Demonstration of Bimolecular Substitution with Anionotropic Rearrangement (S_N2') in 1-Methylallyl Bromide.

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Rates and activation energies for the S_N2 exchange reactions of 1- and 3-methylallyl bromide with lithium bromide in acetone have been measured. The rearrangement of 1-methylallyl bromide under similar conditions has been investigated and shown to be bimolecular, in accordance with the S_N2' mechanism of rearrangement in anionotropic systems. Rates and Arrhenius parameters for the corresponding rearrangement of 3-methylallyl bromide have been inferred from these results. Experiments on the *thermal* rearrangement of these compounds in the pure state are recorded, and a method of stabilising them described.

FOR aliphatic substitution in allyl halides, much evidence has been obtained for the operation of the S_N2 mechanism of substitution (see, especially, Catchpole and Hughes, *J.*, 1948, **4**; Roberts, Young, and Winstein, *J. Amer. Chem. Soc.*, 1942, **64**, 2157; Vernon, *J.*, 1954, 4462) and the S_N1 (Catchpole, Hughes, and Ingold, *J.*, 1948, 8; Vernon, *J.*, 1954, 423). Indeed, as these mechanisms are well established in the general field of nucleophilic aliphatic substitution, it would be surprising if they had no counterparts in the reactions of the allyl compounds. As applied to substitution in allylic systems, the unimolecular mechanism may lead to substitution without (S_N1) or with rearrangement (S_N1') :

$$CH_2{=}CH{-}CHRX \longrightarrow X^- + [CH_2{\frown}CH{-}CHR]^+ \xrightarrow{Y^-} \begin{cases} CH_2{=}CH{-}CHRY & (S_N1) \\ Y{-}CH_2{-}CH{=}CHR & (S_N1') \end{cases}$$

Since the cation-forming step in such a substitution is independent of the nucleophilic reagent, the compound should, ideally, undergo isomeric rearrangement in the same environment if the nucleophilic reagent is omitted. With the S_N2 mechanism, the entering substituent always occupies the position of the displaced atom or group.

Unequivocal evidence for a third mechanism, peculiar to anionotropic systems and involving bimolecular substitution with rearrangement (S_N2'), *viz.*,

$$Y^- + CH_2{=}CH{-}CHRX \longrightarrow [Y{\cdots}CH_2{=}CH{=}CHR{\cdots}X]^- \longrightarrow Y{-}CH_2{-}CH{=}CHR + X^-$$

has been much more difficult to obtain. The mechanism was first suggested as a possibility by Hughes (*Trans. Faraday Soc.*, 1938, **34**, 194) but, until recently, no convincing demonstration had been published. With the simpler allylic halides and nucleophilic reagents, the conditions favouring the S_N2' mechanism are just those which promote S_N2 substitution which then dominates the substitution process, forming a product resistant to attack by either mechanism. Thus, Roberts, Young, and Winstein (*loc. cit.*), on treatment

of 1- and 3-methylallyl chloride with sodium ethoxide in absolute ethanol, obtained at least 96 and 99% respectively of the corresponding ethers, a result confirmed by Catchpole and Hughes (*loc. cit.*) and by de la Mare and Vernon (*J.*, 1953, 3555).

With more complex systems, rearranged products may be obtained but it may not be certain that they have been formed in an S_N2' reaction. A demonstration that the reaction is bimolecular is a necessary part of the evidence. Hence, the conversion of 3-phenylallyl alcohol into 1-phenylallylacetone and of 1-phenylallyl alcohol into 3-phenylallylacetone by Carroll (*J.*, 1940, 1266), quoted by Wilson (*Trans. Faraday Soc.*, 1941, **37**, 631), cannot rank as a demonstration of the S_N2' reaction because this kinetic evidence has not been supplied; furthermore, an alternative interpretation of Carroll's results is available (Kimel and Cope, *J. Amer. Chem. Soc.*, 1943, **65**, 1922). Likewise, bimolecular kinetics have been demonstrated neither for the acid-catalysed rearrangement of allylic alcohols, claimed by Braude (*Ann. Reports*, 1949, **46**, 128) to involve such a mechanism, nor for the rearrangements of the halocodides (Manske and Holmes, " The Alkaloids," Vol. 2, Academic Press, New York, 1952, p. 185; cf. Stork and White, *J. Amer. Chem. Soc.*, 1953, **75**, 4119).

A bimolecular substitution reaction which involves re-arrangement does not necessarily involve the S_N2' mechanism; the rearranged products may result from the rapid intramolecular rearrangement S_Ni' (Ingold, " Structure and Mechanism in Organic Chemistry," Cornell, 1953, p. 596) of the products of substitution without rearrangement. The stability to rearrangement of the starting compound and of possible products of " normal " substitution reactions should therefore be demonstrated. An objection (Dewar, *Bull. Soc. chim.*, 1951, **18**, C43) to the claim (Kepner, Young, and Winstein, *J. Amer. Chem. Soc.*, 1949, **71**, 115) that the formation of rearranged products in the reaction of 1-methyl- and 1-ethyl-allyl chloride with diethyl sodiomalonate in absolute ethanol proceeds by the S_N2' mechanism has been based on this point. Young, Webb, and Goering (*ibid.*, 1951, **73**, 1076) used the formally neutral reagents di- and tri-ethylamine in reaction with 1-methylallyl chloride in benzene and found, with the secondary amine, that a large yield of rearranged products was formed in an apparently bimolecular reaction: the S_N2 substitution product was absent but was prepared by a different method and shown to be stable to rearrangement under the conditions of the reaction. The authors pointed out, however, that the products might be formed by the rearrangement of a pre-formed, hydrogen-bonded complex, a process that might also require second-order kinetics. Young and Clement (*Science*, 1952, **115**, 488) have however now claimed similar rearrangements with tertiary amines where no assistance from hydrogen-bonding is possible.

The most significant tests of the S_N2' mechanism have arisen from deliberate attempts to increase the ratio of the specific rate of the S_N2' reaction to that of the S_N2 reaction by a variety of methods. Hughes and his co-workers (cf. Ingold, *op. cit.*, p. 594) find that the S_N2' rearrangement is easily observable in the reaction of 1-*tert.*-butylallyl chloride with ethoxide ion in absolute ethanol, where the S_N2 reaction is sterically hindered. Alkyl substituents may also increase the S_N2' rate by assisting the displacement of halogen, for de la Mare and Vernon (*loc. cit.*) observed virtually complete rearrangement in the reaction of 1 : 1-dimethylallyl chloride with sodium thiophenoxide, a reaction that is faster than the S_N2 substitution of 1-methylallyl chloride with the same reagent. Independent experiments showed that an S_N2' reaction was undoubtedly under observation. Likewise, additional halogen atoms on the 1-carbon atom appear both to retard the S_N2 substitution and to promote the S_N2' rearrangement, in this case by their inductive effect on the electron density at the 3-carbon atom. Thus de la Mare and Vernon (*J.*, 1952, 3325, 3331, 3628) have observed S_N2' rearrangement in the reactions of 3 : 3-dichloroprop-1-ene and 3 : 3 : 3-trichloro-2-methylprop-1-ene with ethoxide and thiophenoxide ions. In view of the lability of α-chloro-ethers it is most unlikely that an S_N2 substitution followed by an S_Ni' rearrangement is responsible for the rearranged products.

In the simpler alkyl derivatives of allyl halides the S_N2' rearrangement undoubtedly occurs with common nucleophilic reagents, but to such a small extent that an investigation of its characteristics is usually impracticable. In the present work (cf. England and Hughes, *Nature*, 1951, **168**, 1002) the mechanism has been studied in 1-methylallyl bromide by using bromide ions as nucleophilic reagent. This choice ensures that the S_N2 reaction

does not use up the original compound before S_N2' rearrangement has proceeded to a measurable extent: theoretically, the organic bromide is available indefinitely for rearrangment.

$$CH_2{=}CH{\cdot}CHMeBr + Br^- \rightleftharpoons \begin{cases} CH_2{=}CH{\cdot}CHMeBr + Br^- & (S_N2) \\ CH_2Br{\cdot}CH{=}CHMe + Br^- & (S_N2') \end{cases}$$

Furthermore, by using radioactive bromide ion, the kinetic features of the much faster S_N2 reaction can be investigated. 1- and 3-Methylallyl bromide as ordinarily prepared, are unstable compounds rearranging rapidly in the absence of solvent to an equilibrium mixture (Winstein and Young, *J. Amer. Chem. Soc.*, 1936, **58**, 104). We have succeeded in reducing the rate of this type of rearrangement to the point where it does not compete with the heterolytic mechanism S_N2'.

Experimental

Materials.—Acetone was purified by standard methods, and, immediately before use, distilled from anhydrous magnesium perchlorate. For S_N2' runs, diphenylamine was added to the perchlorate in the final distillation, which was conducted in a stream of nitrogen. This procedure prevented the development of colour in the organic bromide solutions (cf. Baker and Nathan, *J.*, 1935, 519).

Radioactive lithium [^{82}Br]bromide was prepared from ammonium bromide after irradiation by the Atomic Energy Research Establishment at Harwell. The product was thoroughly dried and freed from insoluble material before being made up in acetone, inactive bromide being added when necessary. In most cases the [^{80}Br] isotope of 4·4-hr. half-life, which was also produced in the irradiation, had decayed to a negligible activity before the material was used.

All methods of preparation of 1- or 3-methylallyl bromide yield a mixture of the two. 1 : 3-Butadiene was found to be a more convenient starting material than either acraldehyde (Claisen and Tietze, *Ber.*, 1926, **59**, 2344) or crotonaldehyde (Young, Hartung, and Crossley, *J. Amer. Chem. Soc.*, 1936, **58**, 100). Dry diethyl ether (150 ml.) containing a trace of diphenylamine was cooled to −80°. Dry butadiene (54 g., 1 mole) was dissolved in this ether, followed by dry hydrogen bromide (81 g., 1 mole) (*Org. Synth.*, Coll. Vol. 2, Wiley, New York, 1943, p. 338); at this stage, yellow addition products (Archibald and McIntosh, *J.*, 1904, **85**, 925) of hydrogen bromide and ether were formed. The mixture was allowed to warm slowly to room temperature, left for a day, then washed with water and dried ($CaCl_2$). Ether and unchanged butadiene were removed on the water-bath and the residue was fractionated at 93 mm. until the b. p. of 1-methylallyl bromide (31°) was reached. The bromide fraction was then distilled into a trap (−80°) at 1 mm. pressure and room temperature to remove high-boiling impurities. A crude mixture (93 g., 69%) of bromides was obtained. Unfortunately, we were not then aware of the work of Voigt (*J. pr. Chem.*, 1938, **151**, 307) who obtained 81·5% of mixed bromides by passing butadiene into concentrated aqueous hydrogen bromide.

The separation of the bromides requires fractionation below room temperature (Winstein and Young, *loc. cit.*), and a 4 ft., vacuum-jacketed column packed with glass helices was used. The still-head was of conventional design but the condenser and take-off tube (surrounded by thin lead tubing) were kept at about −30° by the circulation of cold alcohol; the receiver was at −80°. To reduce isomerisation, receivers were cleaned with hot chromic acid followed by dilute ammonia solution and water. After being dried, they were heated to redness, flushed with steam, dried again, and cooled in dry nitrogen. Distillations were conducted in a nitrogen atmosphere, usually at 34 mm. pressure. Fractions of 1-methylallyl bromide isolated by this procedure were of constant b. p. but had low and variable purity. The difficulty was avoided by isolating the 3-methylallyl bromide fraction from a mixture stabilised with ammonia (see below) and isomerising this to the equilibrium mixture (Winstein and Young, *loc. cit.*) by 10 mins.' heating on the water-bath. Fractionation of the mixture then yielded pure secondary bromide. More than the theoretical 14% of 1-methylallyl bromide was often isolated from the mixture, as isomerisation occurred in the still-pot. The bromide fractions were brought up to room temperature, and dry ammonia (about 15 ml. to 10 ml. of bromide) was introduced into the air space in the receivers, which were then stored at −80° until required. Physical constants were: 1-methylallyl bromide, b. p. 11·5—11·7°/34 mm., n_D^{26} 1·4599, d_4^{25} 1·2990; 3-methylallyl bromide, b. p. 26·8°/34 mm., n_D^{25} 1·4795, d_4^{25} 1·3372; equilibrium mixture at 25°, n_D^{26} 1·4767. These values compare well with data in the literature (Kharasch, Margolis, and Mayo, *J. Org. Chem.*, 1936, **1**, 393; Winstein and Young, *loc. cit.*) and the bromine content, as determined by quantitative

hydrolysis, had the theoretical value. No evidence for the existence of two forms of 3-methylallyl bromide [but-2-enyl bromide] was obtained (cf. Winstein and Young, *loc. cit.*; Gredy and Piaux, *Bull. Soc. chim.*, **1934**, **1**, **1481**). Glass surfaces, after long contact with bromide mixtures, became opaque.

Stability of 1- *and* 3-*Methylallyl Bromide.*—Previous workers have noted the small and variable stability of these compounds as ordinarily prepared, especially the secondary isomer, observations which were fully confirmed in the present work. However, 3-methylallyl bromide [but-2-enyl bromide] samples remaining in the still-pot after removal of the lower-boiling isomer were often remarkably stable although brown. Such samples resisted isomerisation after 2 hr. at 100° even after addition of charcoal which is a catalyst (Winstein and Young, *loc. cit.*). The same samples were easily isomerised in 10 min. at 100° after fractionation to remove the colour. Secondary bromide samples could be stored indefinitely at −80° under nitrogen without isomerisation, but, on being warmed and transferred to another vessel or to a refractometer at room temperature after a few days at −80°, isomerised very rapidly forming 30% of primary bromide in about 10 min. Freshly distilled samples were usually quite stable enough to allow a careful determination of refractive index at 25°.

Investigations of the stabilising effect of various substances were carried out by sealing about 1 ml. of unstabilised secondary bromide and a trace of the substance in Pyrex tubes (*ca.* 10 cm. long and 8 mm. internal diameter) previously treated in the same manner as the receivers (see above) and heating them in a thermostat at 75° for 30 min. The percentage of isomerisation was measured by the refractive index, which is linear with composition. Freshly distilled samples usually showed about 25% isomerisation under these conditions, but values as small as 5% or as large as 80% were not uncommon. Consequently, in evaluating the effect of any treatment, several "blanks" were used. Filling the tubes with nitrogen or oxygen or adding powdered glass or sodium hydrogen carbonate to the contents was found to have no reproducible effect on the rate of isomerisation. A trace of diphenylamine generally had a slight stabilising effect when the tubes were filled with nitrogen, but quinol, unexpectedly, catalysed the formation of primary bromide. Erratic results were obtained with samples exposed to light during isomerisation but the rate was rather faster when the tubes were evacuated before sealing.

Mayo and Walling (*Chem. Reviews*, **1940**, **27**, **399**) have proposed a free-radical mechanism for the rearrangement of these bromides, mainly on the basis of an observation by Kharasch, Margolis, and Mayo (*loc. cit.*), who found that hydrogen bromide and peroxides in conjunction were powerful catalysts. However, this observation does not necessarily imply that the considerable instability of secondary bromide samples in the absence of added substances is due to the fortuitous presence of these materials. None of the samples which we examined gave a positive test for peroxides, and the effect of quinol (which is among the best inhibitors of abnormal addition of hydrogen bromide to olefins) was opposite to that expected on the above hypothesis.

Concerning the stabilisation of the bromides which was an important feature of the work, by far the most satisfactory results were obtained by introducing a little dry ammonia gas into the the air space in the tubes, a procedure which invariably retarded the isomerisation though not always to the same extent. Some typical results are given below.

Sample	A	B	C
Time at 75° (hr.)	4	0·5	0·5
Isomerisation (%):			
(*a*) untreated	83, 70, 66, 82	25, 17, 26	31, 40, 30
(*b*) treated with ammonia ...	12	9, 5	3, 3

The ammonia technique enabled the secondary bromide to be stored satisfactorily. Samples so treated were stable for weeks in a refrigerator and for several days at room temperature. The bromide was also sufficiently stable in acetone under the conditions of kinetic experiments to enable the test for bimolecular rearrangement to be carried out.

Kinetic Measurements.—S_N2 *Exchange reactions.* For temperatures above −10° thermostats were of conventional design: below this temperature the bath was a large Dewar flask containing alcohol kept at a low temperature by a partially insulated cold-finger containing acetone–solid carbon dioxide mush.

The exchange reactions were carried out in Y-tubes, the separate arms containing, initially, organic bromide (10 ml., *ca.* 0·2M) and lithium bromide (10 ml., *ca.* 0·08M) in acetone. Four tubes were normally used: one, which was allowed to react for about 2 min., served as blank. With 1-methylallyl bromide the reaction was stopped by pouring the Y-tube contents into a

flask at −80°. Acetone and organic bromide were removed at about −20° by a mechanical pump, leaving lithium bromide as a white deposit to which two separate 5-ml. portions of acetone were added and evaporated off, ensuring complete removal of the organic bromide. The lithium bromide samples, including one from the original acetone solution, were made up to a suitable volume in water and counted in a 10-ml. liquid counter (Twentieth Century Electronics, Type M6) connected to a conventional high-voltage supply and scaling circuit. The samples were each counted for two periods of 12 min. separated by some 80 min., and for a further 12 min. period if, owing to statistical fluctuations, the slope of the log counts/min.–time plot differed considerably from that characteristic of the 36·2 hr. half-life. Parallel straight lines were drawn through the groups of points for each sample, and the relative activities thereby estimated at the same time, after correction for the small background count. A total of at least 10^4 counts was recorded for each. The concentration of lithium bromide was then determined by weight titration, enabling the specific activity of each sample to be calculated.

3-Methylallyl bromide reacted too quickly to allow the evaporation technique to be used and, instead, the reaction was stopped by pouring the Y-tube contents into water (15 ml.) and pentane (40 ml.) in a separating funnel. After shaking, the water layer was run off into more pentane (20 ml.), shaken again, separated, and evaporated to dryness, and the lithium bromide was dissolved in water and estimated.

Specific rates of the exchange reactions were calculated by a modification of Le Roux and Sugden's equation (*J.*, 1939, 1279), *viz.*,

$$k_2 = 2{\cdot}303\{\log_{10}[1 - z_1(1 + b/a)]/[1 - z_2(1 + b/a)]\}/(a + b)(t_2 - t_1)$$

where a and b are the concentrations of organic and inorganic bromide respectively, corrected for solvent expansion or contraction from Thorpe's data (*J.*, 1880, **37**, 212), and $z = (1 - y)$, where y is the specific activity of a sample of recovered lithium bromide compared with that of the original sample taken as unity. Data for a typical run (1-methylallyl bromide at 30·0°) are given in Table 1 where k_2 is expressed in l mole.$^{-1}$ sec.$^{-1}$; $a = 0{\cdot}0994$M, $b = 0{\cdot}0430$M.

TABLE 1.

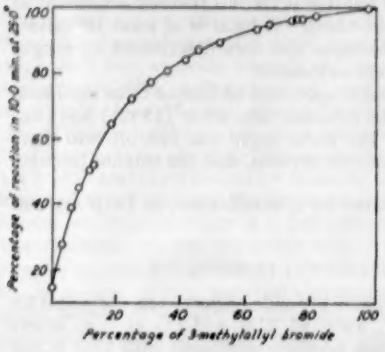
Aqueous lithium bromide.					*Aqueous lithium bromide.*				
t (sec.)	ct./min.	Concn.	z	10^3k_2	t (sec.)	ct./min.	Concn.	z	10^3k_2
115	2702	0·0435	0·0373	—	4735	2350	0·0647	0·4364	1·41
1820	2460	0·0493	0·2263	1·39	Original LiBr	2494	0·0387	Mean k_2	1·39
3015	3064	0·0699	0·3204	1·36					

In another run at the same temperature with $b = 0{\cdot}0254$M the mean rate was $1{\cdot}66 \times 10^{-3}$. The reaction thus shows a salt effect of the same sign and magnitude as that observed for saturated bromides by de la Mare (Thesis, University of London, 1948) and by Evans and Sugden (*J.*, 1949, 270), and all results were corrected to a standard concentration (0·04M). A similar salt effect was observed with 3-methylallyl bromide.

S_N2' Reactions. Attempts to follow the rearrangement by isolating the organic bromide mixture and measuring the refractive index were unsuccessful because thermal isomerisation always occurred during the removal of the acetone solvent by fractional distillation. However, no products other than 3-methylallyl bromide were isolated in the reaction of 1-methylallyl bromide with lithium bromide at temperatures up to 80°. The pseudo-first-order kinetics of an S_N2' rearrangement of this type are well suited to a dilatometric study, but the small density difference of the two isomers again made accurate measurements impossible. The method finally used depended on the large difference in the rates of S_N2 substitution of the two bromides: for convenience radioactive bromide ion was chosen as nucleophilic reagent. The very rapid exchange of the primary bromide with this reagent at 25° allowed conditions to be chosen for the kinetic analysis under which further S_N2' rearrangement was negligible though it was not great enough to allow exchange of the secondary bromide to be neglected. Consequently, an empirical curve was prepared connecting the composition of bromide mixtures with the extent of exchange with radioactive lithium bromide under standard conditions (see Figure). The results were obtained as follows. Mixtures of the pure bromides (total concentration *ca.* 0·2M) were made up in acetone. Aliquot parts (10 ml.) of these solutions were mixed at 25° with the same volume of radioactive lithium bromide (0·02M): after 10·0 min. the reaction was stopped by rapid quenching at −80°. The specific activity of the lithium bromide which was isolated by evaporation was measured as above, greater precision being secured by recording more counts and using

more than one original sample. The value of z was computed for each mixture and multiplied by $100(1 + b/a)$, where a is the total organic bromide concentration, to obtain a function which increased from 0 at zero exchange to 100 when equilbrium between inorganic and organic bromides was attained. This " percentage reaction " is plotted against the percentage of 3-methylallyl bromide for 20 different mixtures in the Figure.

For the S_N2' rate measurements, aliquot parts (10 ml.) of 1-methylallyl bromide (0·5M) and lithium bromide (usually 0·08M) were mixed at room temperature and allowed to react in sealed Monax test-tubes. Precautions were taken to exclude oxygen. After reaction, the mixtures were carefully evaporated at low pressure to separate lithium bromide, the distillate being collected in a trap at −80°. Further acetone (5 ml.) was added to and evaporated off the lithium bromide deposit to remove all traces of organic bromide and yield as distillate an acetone solution (*ca.* 0·2M) of the mixed bromides. Precautions were taken to exclude moisture. An aliquot portion of this distillate was then allowed to react with radioactive lithium bromide exactly as above; a second aliquot portion was completely hydrolysed and titrated for bromide ion to measure the exact concentration of organic bromides.



Both bromides were found to produce, after 260 hr. at 50·0°, a mixture of the same composition within experimental error, and eight separate determinations of this composition, using both pure bromides and thermal equilibrium mixtures as starting materials with 0·04M-lithium bromide, yielded 75·0% as the mean equilibrium percentage of 3-methylallyl bromide. In the same time, 1-methylallyl bromide, in the absence of lithium bromide, yielded 4·7 and 6·7% of 3-methylallyl bromide, and this compound yielded, very approximately, 14% and 17% of 1-methylallyl bromide. To prove the absence of hydrogen bromide (which would be recorded as 3-methylallyl bromide by the method of analysis) a reaction mixture at equilibrium was separated from lithium bromide and allowed to react with radioactive lithium bromide at −80°. There was no exchange of bromide within experimental error.

The rearrangement of 1-methylallyl bromide was found to have the kinetic form of a reversible, pseudo-first-order reaction; second-order specific rates were calculated from the equation $k_2 = 2{\cdot}303 \times 0{\cdot}75[\log_{10}(x_e - x_1)/(x_e - x_n)]/b(t_n - t_1)$, where b is the lithium bromide concentration, x is the concentration of 3-methylallyl bromide at time t, and x_e its concentration at equilibrium. The reaction was followed, until at least 48% of primary bromide was produced, at four different temperatures. In no case was any drift of the constant k_2 observed. Details of a run at 50·0° are given in Table 2, where k_2 is in l. mole^{-1} sec.$^{-1}$.

TABLE 2.

Initial concns.: 1-methylallyl bromide, 0·236M; LiBr, 0·0400M.

Tube No.	Time (min.)	3-Methylallyl-bromide, %	10^5k_2	Tube No.	Time (min.)	3-Methylallyl-bromide, %	10^5k_2
1	12	1·6	—	5	1265	38·7	17·6
2	143	6·6	16·8	6	1598	44·8	17·5
3	317	13·0	17·3	7	1913	48·3	16·6
4	548	20·3	17·1			Mean	17·2

Kinetic analysis (radioactive LiBr, 0·01020M):

Tube No.	*Aqueous* LiBr a	ct./min.	Concn. $\times 10^5$	$z(1 + b/a)$ $\times 100$	Tube No.	*Aqueous* LiBr a	ct./min.	Concn. $\times 10^5$	$z(1 + b/a)$ $\times 100$
1	0·0961	6783	1120	22·3	5	0·0986	2597	1367	82·7
2	0·0998	4742	984·8	40·3	6	0·0982	2663	1587	86·0
3	0·0997	4090	1097	56·1	7	0·0950	2407	1526	87·7
4	0·0989	2827	959·4	67·5	Original LiBr		4618	608·6	—

The effect of varying the initial lithium bromide concentration on the rate of the reaction at 60·2° is shown in Table 3.

TABLE 3.

Initial concn., 1-methylallyl bromide, 0·247M; k_2 in l. mole^{-1} sec.$^{-1}$.

Tube No.	b	Time (min.)	3-Methylallyl bromide, %	10^5k_2	Tube No.	b	Time (min.)	3-Methylallyl bromide, %	10^5k_2
1	0·0101	970	29·4	63·5	5	0·0503	199	23·3	46·5
2	0·0201	1245	49·9	54·7	6	0·0603	172	22·0	41·8
3	0·0302	343	25·6	50·4	7	0·0804	120	19·2	38·3
4	0·0402	245	22·4	45·0	8	0·1005	98	20·4	40·3

DISCUSSION

The results in Table 3 show that the rearrangement has an order of approximately 0·75 with respect to lithium bromide. That this order should be less than unity is not unexpected since Evans and Sugden (*loc. cit.*), investigating the S_N2 exchange reactions of *n*-butyl and *sec.*-octyl bromides with lithium bromide in acetone, found a similar effect which they attributed to incomplete dissociation of lithium bromide in this solvent, and de la Mare (Thesis, University of London, 1948) has observed a similar " dilution effect " with *tert.*-butyl bromide. It is therefore concluded that the rearrangement is bimolecular.

In the reactions of alkyl halides with nucleophilic reagents the possible elimination of hydrogen halide must always be borne in mind. In the present case the possibility that the rearranged products are due to elimination of hydrogen bromide followed by re-addition may be discounted since 1-methylallyl halides do not readily undergo elimination reactions even with reagents whose nucleophilic affinity for hydrogen is very much more marked than that of bromide ion. For example, Vernon (*J.*, 1954, 4462) found that only 10% of butadiene was formed in the reaction of 1-methylallyl chloride with sodium ethoxide. We therefore conclude that 1-methylallyl bromide undergoes rearrangement by the S_N2' mechanism in the presence of lithium bromide.

The exchange reactions of the bromides with radioactive lithium bromide should show first-order kinetics in a single run whatever the mechanism (Duffield and Calvin, *J. Amer. Chem. Soc.*, 1946, **68**, 557) but, since the dependence of the rate on lithium bromide concentration is similar to that mentioned above, the S_N2 mechanism is indicated, a conclusion which is confirmed by the much greater rate of the primary isomer (cf. Vernon, *J.*, 1954, 423). Rearrangement does not interfere with the exchange measurements since it can be calculated that, at most, 0·5% of primary bromide was formed by the S_N2' reaction during measurement of the S_N2 exchange. The kinetic data (k_2 and A_2 in l. mole^{-1} sec.$^{-1}$) and Arrhenius parameters are given below. In the final column, rates are compared at 25° by interpolation or extrapolation.

Allyl bromide	Temp.	10^5k_2	E_A (kcal. mole^{-1})	$\log_{10} A_2$	10^5k_2 (25°)
1-Methyl- (S_N2)	30·00°	142	16·5	9·06	879
	24·80	86·6			
	16·05	36·7			
	−6·20	3·44			
1-Methyl- (S_N2')	75·15	157	19·4	9·40	14·9
	60·20	44·2			
	50·00	17·2			
	30·05	2·42			
3-Methyl- (S_N2)	−18·80	198	14·7	9·93	141,000
	−27·25	71·3			
	−33·10	34·9			
3-Methyl (S_N2')	—	—	*ca.* 19	*ca.* 9	5

The S_N2 substitution of 1-methylallyl bromide is 60 times faster than the corresponding S_N2' rearrangement at 25° and this difference arises largely from a difference of 3 kcal. in the activation energy. It is likely that the bimolecular substitution reactions of all 1-substituted allyl halides involve at least a small percentage of rearrangement, which, in 1-methyl halides, is just beyond the usual limit of detection in a product analysis. It is also understandable that some derivatives (cf. de la Mare and Vernon, *locc. cit.*) have been found to react exclusively by the S_N2' mechanism.

The corresponding ratio of rates in 3-methylallyl bromide is much greater (28,000 : 1) and this is due largely to the facilitation of the S_N2 reaction by the 3-methyl group. The

contribution of the S_N2' mechanism to the bimolecular reactions of halides substituted only in the 3-position may generally be expected to be quite negligible.

The author is deeply indebted to Professor C. K. Ingold, F.R.S., and to Professor E. D. Hughes, F.R.S., who suggested this approach to the study of the S_N2' reaction, for their unfailing help and encouragement. Thanks are also due to Dr. P. B. D. de la Mare and Dr. C. A. Vernon for much useful discussion. The award of a Post-Graduate Scholarship in Science by the University of New Zealand is gratefully acknowledged.

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A Derivative of cyclo*Heptatrienylium (Tropylium) Bromide.*

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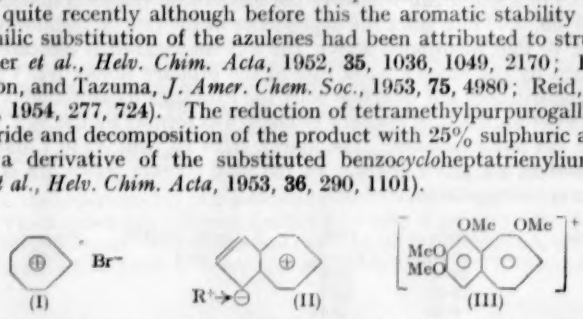
[Reprint Order No. 6069.]

The action of bromine on β-*cyclo*heptatrienecarboxylic acid yields an adduct which loses hydrogen bromide when heated to give carboxy*cyclo*heptatrienylium bromide (VI), a polar compound containing ionic bromine. The properties of this product are similar to those of the parent *cyclo*heptatrienylium bromide (I) (Doering and Knox, *J. Amer. Chem. Soc.*, 1954, **76**, 3203). Attempts to prepare the latter bromide (I) by Curtius degradation of α-*cyclo*heptatrienecarboxylic acid led to the formation of α-*cyclo*heptatrienylurethane, a non-polar compound in which the ring carbon–nitrogen bond is easily severed by hydrolysis.

THE aromatic character of tropolones and tropones is attributed to the presence of the *cyclo*heptatrienylium cation in the molecules. Simple salts derived from this cation were unknown until quite recently although before this the aromatic stability and the course of the electrophilic substitution of the azulenes had been attributed to structures such as (II) (Heilbronner *et al.*, *Helv. Chim. Acta*, 1952, **35**, 1036, 1049, 2170; 1954, **37**, 2018; Anderson, Nelson, and Tazuma, *J. Amer. Chem. Soc.*, 1953, **75**, 4980; Reid, Stafford, *et al.*, *Chem. and Ind.*, 1954, 277, 724). The reduction of tetramethylpurpurogallin with lithium aluminium hydride and decomposition of the product with 25% sulphuric acid gave a salt formulated as a derivative of the substituted benzo*cyclo*heptatrienylium cation (III) (Eschenmoser *et al.*, *Helv. Chim. Acta*, 1953, **36**, 290, 1101).



(I) (II) (III)

The preparation and some of the properties of *cyclo*heptatrienylium bromide (I) have recently been described by Doering and Knox (*J. Amer. Chem. Soc.*, 1954, **76**, 3203). It was obtained by heating the dibromide from *cyclo*heptatriene and was a deliquescent solid, m. p. 203°, insoluble in non-polar organic solvents and generally possessing properties consistent with its formulation as a salt. Actually its preparation had been described many years ago by Merling (*Ber.*, 1891, **24**, 3122), who, without appreciating its significance, had observed the formation of a crystalline residue in the distillation of *cyclo*heptatriene dibromide. The product as obtained by Doering and Knox (*loc. cit.*) contained ionic bromine, gave *cyclo*heptane on hydrogenation, and was converted, by reaction with aqueous sodium hydrogen carbonate, into di*cyclo*heptatrienyl ether. Dauben (Abs. Amer. Chem. Soc. 126th Meeting, 1954, p. 18-o) has also claimed to have prepared (I) from the dibromide of *cyclo*heptatriene.

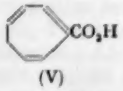
Several possible synthetic routes to (I) have been examined in our laboratories, *e.g.*, oxidation of *cyclo*heptatriene with *N*-bromosuccinimide (cf. Dryden and Burgert, *ibid.*, p. 22-o), reduction of tropone, and degradation of the various isomeric *cyclo*heptatrienecarboxylic acids. Reduction of 2 : 4 : 7-tribromotropone with lithium aluminium hydride

gave an unsaturated dibromo-alcohol $C_7H_{10}OBr_2$ in which reduction of the ring had occurred (cf. Cook, Raphael, and Scott, *J.*, 1952, 4416). The structure of this product was not fully elucidated in view of the outcome of the experiments with the *cyclo*heptatrienecarboxylic acids.

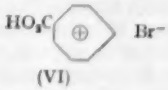
Buchner's classical work (*Ber.*, 1898, **31**, 2241; 1901, **34**, 897) on the ring expansion of benzene with diazoacetic ester has been re-examined by Grundmann and Ottmann (*Annalen*, 1953, **582**, 163) who, on the basis of ultraviolet spectra and mode of formation, revised the structures assigned by Buchner to the four *cyclo*heptatrienecarboxylic acids. Thus the structure of the α-isomer, m. p. 71° (IV; R = CO_2H), was deduced on the basis of the weak maximum in the absorption curve at 260 mμ (log ε 3·40), whereas the other double-bond isomers absorb at *ca.* 280 mμ (log ε 3·52—3·76).

α-*cyclo*Heptatrienecarboxylic acid was selected initially for experiments on the replacement of the carboxy-group because it was felt that the absence of double bonds conjugated with the substituent would lessen the tendency of the products to rearrange. However, attempts to replace the carboxy-group by bromine, by direct bromination of the silver salt or by use of silver trifluoroacetate and bromine, were unsuccessful, as were attempted Schmidt reactions. By the Curtius reaction the acid chloride (IV; R = COCl) gave the *iso*cyanate and urethane (IV; R = NH·CO_2Et), the latter being a pale yellow oil, $C_{10}H_{13}O_2N$, b. p. 85—90°/0·4 mm. In order to show that no rearrangement of double bonds had occurred during the formation of the acid chloride it was converted into the amide (IV; R = CO·NH_2), the ultraviolet absorption of which was very nearly identical with that of the original acid. The infrared spectrum of the urethane showed a strong band at 3322 $cm.^{-1}$, corresponding to the NH group and thus excluding the possibility of tautomerism. Although the volatility and physical nature of the urethane clearly indicated the covalent structure (IV; R = NH·CO_2Et) (cf. the methyl ether, Doering and Knox, *loc. cit.*) rather than a polar structure of type (I), certain of the physical and chemical properties of the compound indicates that the carbon–nitrogen bond was quite weak. The ultraviolet absorption (max. at 270—271 mμ; log ε 3·88) was more intense than that of the original amide (IV; R = CO·NH_2) (259—260 mμ; log ε 3·42) and somewhat resembled that of *cyclo*heptatrienylium bromide (275 mμ; log ε 3·65; Doering and Knox, *loc. cit.*).

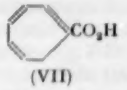
(IV)



(V)



(VI)



(VII)

The strength of the carbon–nitrogen covalent bond in an amine or urethane can be gauged by the ease of its hydrolysis. Thus the simple aliphatic and aromatic amines resist hydrolysis under extreme conditions whereas (triphenylmethyl)amine gives 85% of the theoretical amount of ammonium chloride after hydrolysis with N/20-hydrochloric acid at 100° for 90 minutes (Kharasch and Howard, *J. Amer. Chem. Soc.*, 1934, **56**, 1370). Treatment of the urethane derived from α-*cyclo*heptatrienecarboxylic acid with N/100-acetic acid at 100° for 2 hours gave 30% of free urethane; even contact with moist solvents, especially alcohols at room temperature, yielded appreciable amounts of free urethane but other hydrolysis products have not been isolated. Triphenylmethylurethane, Ph_3C·NH·CO_2Et, with N/10-acetic acid at 100° for 4 hours gave only 9% of free urethane. The α-*cyclo*heptatrienylurethane darkened noticeably in air even at room temperature and when heated it was converted into a brown polymeric substance.

In experiments with β-*cyclo*heptatrienecarboxylic acid (V) (Grundmann and Ottmann, *loc. cit.*) it was found that it readily formed a colourless dibromide, m. p. 145—146° (Einhorn *et al.*, *Ber.*, 1893, **26**, 331, and *Annalen*, 1894, **280**, 124, give m. p. 135° for an isomeric dibromo*cyclo*heptadienecarboxylic acid) but, when the crude addition product was heated under reduced pressure, hydrogen bromide was liberated and carboxy*cyclo*heptatrienylium bromide (VI) was obtained in low yield [0·8%; the figure of 8% given by Johnson and Tisler (*Chem. and Ind.*, 1954, 1427) in a preliminary announcement was a typographical error]. The same product was obtained, although in even smaller yield, from γ-*cyclo*heptatrienecarboxylic acid (VII) (Grundmann and Ottmann, *loc. cit.*) by a similar process

although not from the esters of (V) or (VII). The formation of (VI) from two isomers of *cyclo*heptatrienecarboxylic acid constitutes supporting evidence for the structure assigned to the product as double-bond rearrangement would not be expected under the experimental conditions employed.

The acid (VI) was a dull yellow crystalline solid, easily soluble in water and alcohols and insoluble in ether, benzene, and light petroleum. It was obtained anhydrous and as a monohydrate and was a strong acid (p*K* 3·3). It charred at about 180° but did not melt. Addition of silver nitrate to an aqueous solution of the acid caused an immediate precipitate of silver bromide and the structure (VI) followed from hydrogenation of the acid in the presence of platinum, four mols. of hydrogen being absorbed and *cyclo*heptanecarboxylic acid obtained. There was therefore a close relation between the properties of (VI) and those of the unsubstituted bromide (I) (Doering and Knox, *loc. cit.*). Other reactions of (VI) are being studied.

Of the various *cyclo*heptatrienyl derivatives, C_7H_7X, which have been prepared, only the halides (X = Cl and Br) are polar compounds. The methyl ether, amine, and urethane as well as di*cyclo*heptatrienyl ether are all covalent compounds and it appears that the seven-membered alicyclic cation needs an anion derived from a relatively strong acid, HX, for the formation of a stable salt.

Experimental

Unless otherwise stated, ultraviolet spectra were determined in 95% EtOH, and infrared spectra on Nujol mulls.

Reduction of 2 : 4 : 7-*Tribromotropone.*—Lithium aluminium hydride (496 mg.) was suspended in dry tetrahydrofuran (10 c.c.) and cooled to −30°. A solution of 2 : 4 : 7-tribromotropone (1·06 g.) (Nozoe, Kitahara, Ando, Masumune, and Abe, *Sci. Rep. Tôhoku Univ.*, 1952, **36**, 166) in dry tetrahydrofuran (30 c.c.) was added dropwise with stirring during 30 min. and the mixture stirred for a further 2 hr. at −20° to −30°, then for 30 min. at room temperature. The product was decomposed by the addition of wet ether (50 c.c.), followed by water (10 c.c.), and then divided into equal portions A and B. Solution A was acidified with 4N-sulphuric acid (15 c.c.) and extracted with ether (3 × 20 c.c.). The ethereal extract was dried and the solvent removed, leaving a light brown oil (279 mg.) which slowly crystallised. The aqueous layer was made alkaline and again extracted with ether. This ethereal extract was dried and evaporated but left only a small amount (4 mg.) of brown gum. Solution B was made alkaline with sodium hydroxide (1·3 g.) and extracted with ether (3 × 20 c.c.). After drying of the ethereal extract and removal of the solvent, a light brown solid (337 mg.) remained. The aqueous layer was acidified with hydrochloric acid and again extracted with ether as before, but only a small quantity (7 mg.) of a brown gum was obtained. The two solid extracts were combined and distilled at 0·5 mm., a colourless solid *dibromide* (567 mg.) being obtained which after crystallisation from benzene–light petroleum (b. p. 60—80°) formed colourless needles, m. p. 98° (Found: C, 31·4; H, 3·8. $C_7H_{10}OBr_2$ requires C, 31·15; H, 3·7%).

α-cyclo*Heptatrienecarboxylic Acid* (IV; R = CO_2H) *and its Derivatives.*—The acid, m. p. 71°, was prepared according to Grundmann and Ottmann (*loc. cit.*). Light absorption: max. at 260 mμ (log ε 3·40); and in concentrated sulphuric acid: max. at 226, 284, and 330 mμ (log ε 4·37, 3·55, and 3·39 respectively). The infrared spectrum showed max. at 2632, 2532, 1701, 1605, 1414, 1326, 1294, 1277, 1212, 1179, 1095, 1047, 957, 926, 902, 880, 806, 775, 758, 717, and 676 cm.$^{-1}$.

The acid chloride, b. p. 74°/4 mm., was prepared by the action of thionyl chloride, and converted into the amide which formed colourless plates, m. p. 128—129° (Buchner, *Ber.*, 1897, **30**, 632, gives m. p. 129°), on sublimation and crystallisation from aqueous methanol. Light absorption: max. at 259—260 mμ (log ε 3·42). Infrared spectrum: max. at 3322, 3175, 1669, 1637, 1595, 1538, 1447, 1412, 1316, 1294, 1221, 1209, 1181, 1131, 1099, 1048, 1027, 996, 959, 944, 935, 905, 870, 812, 761, 728, and 706 cm.$^{-1}$.

Curtius Reaction with α-cyclo*Heptatrienecarboxylic Acid Chloride* (IV; R = COCl).—(*a*) Activated sodium azide (448 mg.) (Smith, *Org. Reactions*, 1946, **3**, 382) was added to a solution of the acid chloride (866 mg.) in dry xylene (7 c.c.). The mixture was heated at 114°, nitrogen (115 c.c., 92%) being evolved during 5 hr. The mixture was cooled, the inorganic salts were separated, and the filtrate and xylene washings (2 × 5 c.c.) treated with 10N-hydrochloric acid (1·7 c.c.) and heated at 100°. The solvent was removed *in vacuo*, leaving a yellow semicrystalline

gum which gave a brown amorphous solid on attempted crystallisation from methanol–ether. The solid was dissolved in methanol and precipitated by addition of ether several times until a colourless powder (214 mg.) was obtained which proved to be ammonium chloride (71% calc. on the acid chloride).

(*b*) Sodium azide (570 mg.) was treated with α-*cyclo*heptatrienecarbonyl chloride (1·23 g.) in dry xylene (7 c.c.) as in the previous experiment. The salts were separated from the cooled solution and washed with dry ethanol (3 × 2 c.c.), and the combined filtrates heated at reflux temperature for 2 hr. with more dry ethanol (20 c.c.). After removal of the solvent *in vacuo* at 100°, there remained a light brown viscous oil which was distilled at 87° (bath temp.)/0·4 mm. A very volatile colourless solid was obtained together with a pale yellow oil and a dark brown solid residue. The volatile solid formed colourless plates (23 mg.), m. p. 48—49°, after crystallisation from light petroleum (b. p. 60—80°), and the m. p. was not depressed when the product was mixed with ethyl carbamate (Found: C, 40·65; H, 8·0; N, 15·9. Calc. for $C_3H_7O_2N$: C, 40·45; H, 7·9; N, 15·7%). The oily N-cyclo*heptatrienylurethane* (458 mg.) was redistilled for analysis (Found: C, 67·0; H, 7·5; N, 7·8. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3; N, 7·8%). Light absorption: max. at 270—271 mμ (log ε 3·88); in sulphuric acid: max. at 226, 265, 344, and 392—393 mμ (log ε 3·97, 3·64, 3·16, and 3·22 respectively). The infrared spectrum of the liquid itself showed max. at 3322, 2985, 2890, 2841, 1715, 1634, 1524, 1481, 1445, 1379, 1316, 1235, 1171, 1095, 1056, 1005, 946, 923, 889, 852, 829, 797, 772, and 709 cm.$^{-1}$. The urethane was unstable in the presence of air or moisture but could be preserved at 0·3 mm. in a sealed tube. Moist solvents, especially methanol, caused hydrolysis to ethyl carbamate and a dark brown gum. The oil was soluble in most organic solvents except light petroleum, and insoluble in water, and with concentrated sulphuric acid it gave a strong yellow colour which disappeared on dilution with water.

(*c*) In other experiments the crude reaction products from sodium azide and α-*cyclo*heptatrienecarbonyl chloride in xylene solution were treated with ferric chloride in the presence of hydrogen chloride, hydrogen chloride alone, and 60% perchloric acid, but in no case were pure products isolated other than ammonium chloride.

Reactions of α-cyclo*Heptatrienylurethane* (IV; R = NH·CO_2Et).—(a) *Hydrolysis*. Oxygen-free nitrogen was led through a suspension of the urethane in N/100-acetic acid at 100°. After 2 hr. a clear solution was obtained which was extracted with ether (3 × 20 c.c.). Evaporation of the aqueous phase at 100° in a vacuum gave a pale brown gum (2 mg.). The ethereal extract was dried and the solvent removed, to leave a yellow oil which on distillation at 107° (bath-temp.)/0·6 mm. gave a pale yellow oil (63 mg.) and colourless plates (19 mg., 30%), m. p. 49—50°, identical with ethyl carbamate.

(b) No solid products were obtained from reactions of the urethane in dry ether with 60% perchloric acid, concentrated sulphuric acid, anhydrous picric acid, anhydrous trifluoroacetic acid, or dry hydrogen chloride. Likewise no pure products were isolated from reactions of the urethane with 10% methanolic auric chloride alone or saturated with hydrogen chloride, methanolic picric acid, or 50% hydrobromic acid in acetic acid at 100°.

Triphenylmethylurethane.—A solution of triphenylmethylamine (5 g.) (Elbs, *Ber.*, 1884, **17**, 701) in dry ether (40 c.c.) was caused to react with ethyl chloroformate (1·1 g.) at the b. p. for 3 hr. during which a colourless precipitate formed. The ether was evaporated and the residue extracted with hot light petroleum (b. p. 60—80°; 3 × 50 c.c.), leaving (triphenylmethyl)amine hydrochloride as colourless crystals (2·67 g.), m. p. 243—244°. The solvent was removed from the petroleum extracts and the residue crystallised from aqueous methanol, to give colourless plates (2·81 g., 91% calc. on half the amount of triphenylmethylamine used), m. p. 110—111° (Found: C, 79·7; H, 6·2; N, 4·5. $C_{22}H_{21}O_2N$ requires C, 79·7; H, 6·4; N, 4·2%).

A solution of this *urethane* (282 mg.) in N/10-acetic acid (10 c.c.) and methanol (5 c.c.) was heated under reflux for 4 hr. The solvents were removed *in vacuo* and the glassy residue was sublimed at 0·5 mm., to give plates (7 mg., 9%), m. p. 49—50°, not depressed when mixed with ethyl carbamate. The residue from the sublimation was crystallised from aqueous methanol to give colourless plates (214 mg., 76%) of triphenylmethylurethane, m. p. 110—111°.

β-cyclo*Heptatrienecarboxylic Acid* (V) *and its Derivatives*.—The acid, m. p. 56°, was prepared according to Grundmann and Ottmann (*loc. cit.*). Light absorption: max. at 275—277 mμ (log ε 3·76). The infrared spectrum showed max. at 2653, 2532, 1695, 1616, 1538, 1408, 1335, 1282, 1235, 1186, 1099, 1049, 1021, 976, 965, 949, 905, 889, 798, 765, 733, and 668 cm.$^{-1}$.

The acid chloride, b. p. 93°/7 mm., n_D^{18} 1·5763, was prepared by the action of thionyl chloride and converted into the amide which sublimed at 90°/0·5 mm. and crystallised from ether as colourless plates, m. p. 97—98° (Buchner and Lingg, *Ber.*, 1898, **31**, 402, give m. p. 98°) (Found:

C, 71·1; H, 6·9. Calc. for C_8H_9ON: C, 71·1; H, 6·7%). Light absorption: max. at 274 mμ (log. ε 3·75).

The *dibromide*, prepared by the addition of bromine (1 mol.) to the acid in chloroform solution, formed colourless plates, m. p. 145—146° (decomp.) after crystallisation from ethanol (Found: C, 32·9; H, 2·6. $C_8H_8O_2Br_2$ requires C, 32·5; H, 2·7%). Hydrogenation of the product over platinum yielded *cyclo*heptanecarboxylic acid, identified as the amide, m. p. 195°, not depressed on admixture with an authentic specimen (Bartels-Keith, Johnson, and Langemann, *J.*, 1952, 4461).

*Carboxy*cyclo*heptatrienylium Bromide* (VI).—A solution of bromine (0·88 c.c., 0·8 mol.) in carbon tetrachloride (10 c.c.) was added dropwise to a cooled solution (ice) of β-*cyclo*heptatrienecarboxylic acid (3 g.) (Grundmann and Ottmann, *loc. cit.*) in carbon tetrachloride (20 c.c.). The solvent was then removed from the pale yellow solution under reduced pressure and the gummy residue heated at 80—90°/10^{-5} mm. for 2 hr. After cooling, dry ether (25 c.c.) was added and the solid insoluble *bromide* separated. It was dissolved in the least volume of dry ethanol and precipitated by addition of ether, being obtained as small dull yellow crystals (40 mg.) (Found: C, 41·0; H, 4·3. $C_8H_7O_2Br,H_2O$ requires C, 41·2; H, 3·9. Found, in a sample dried at 80—90°/0·01 mm.: C, 45·0; H, 3·6; Br, 36·95. $C_8H_7O_2Br$ requires C, 44·7; H, 3·3; Br, 37·15%). The bromide chars at about 180° but does not melt below 300°; pK_a 3·29. It is very soluble in water and alcohols but insoluble in non-polar organic solvents. Addition of silver nitrate to an aqueous solution gives an immediate precipitate of silver bromide. Light absorption in water: max. at 272—273 mμ (log ε 3·68) and min. at 246—247 mμ (log ε 3·52). The infrared spectrum (KBr plate) showed max. at 3279, 3003, 1980, 1715, 1631, 1563, 1531, 1477, 1443, 1387, 1366, 1280, 1258, 1239, 1212, 749, and 686 cm.$^{-1}$. Hydrogenation of an ethanolic solution of the bromide over a platinum catalyst caused the absorption of 4 mols. of hydrogen and the *cyclo*heptanecarboxylic acid so formed was identified as its amide, m. p. 195°, as above.

By a similar method, the liquid γ-*cyclo*heptatrienecarboxylic acid (VII) (1 g.) (Grundmann and Ottmann, *loc. cit.*) reacted with bromine (0·3 c.c., 0·8 mol.) and was treated as in the previous experiment. Carboxy*cyclo*heptatrienyl bromide (10 mg.), identical with that obtained as above, was isolated from the product.

Grateful acknowledgement is made to Professor Sir Alexander Todd, F.R.S., for his interest and to the British Council for a Scholarship (to M. T.).

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NOTES.

Dissociation Constants of the Dihydrolysergic Acids.

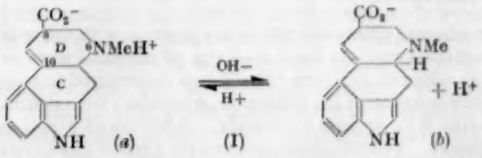
By J. B. STENLAKE.

[Reprint Order No. 5812.]

FOR reasons detailed elsewhere (*Chem. and Ind.*, 1953, 1089) and contrary to Cookson (*ibid.*, p. 337), Stenlake deduced from the $pK'_{a,2}$ values of lysergic (7·68, 7·96) and *iso*lysergic acid (I) (8·31, 8·60) (see Craig, Shedlovsky, Gould, and Jacobs, *J. Biol. Chem.*, 1938, **125**, 289) that the former acid, being the weaker, has the conformation in which the carboxyl group and $N_{(6)}$ are remote from each other; it is here assumed that in both acids ring D has the semi-chair structure (cf. Raphael and Stenlake, *Chem. and Ind.*, 1953, 1286; Barton, Cookson, Klyne, and Shoppee, *ibid.*, 1954, 21); the carboxyl group would then be axial in *iso*lysergic and equatorial in lysergic acid. This interpretation is supported by comparable assignments of structure to the isomeric cytidylic and adenylic acids (Cavalieri, *J. Amer. Chem. Soc.*, 1953, **75**, 5268) based on dissociation constants, this being confirmed by independent chemical and physical evidence (Brown, Fasman, Magrath, Todd, Cochran, and Woolfson, *Nature*, 1953, **172**, 1184; Michelson and Todd, *J.*, 1954, 34).

Cookson (*loc. cit.*) showed by conformational analysis, based on the relative stabilities of the dihydrolysergic acids, that the carboxyl group is equatorial in dihydrolysergic acid I and dihydro*iso*lysergic acid II and axial in dihydro*iso*lysergic acid I. Thus on the

assumption that the now saturated ring D adopts the more stable chair conformation as in other piperidine derivatives (Sparke, *Chem. and Ind.*, 1953, 759; Bose and Chaudhuri, *Nature*, 1953, **171**, 652) the carboxyl group will be more remote from $N_{(6)}$ in dihydrolysergic

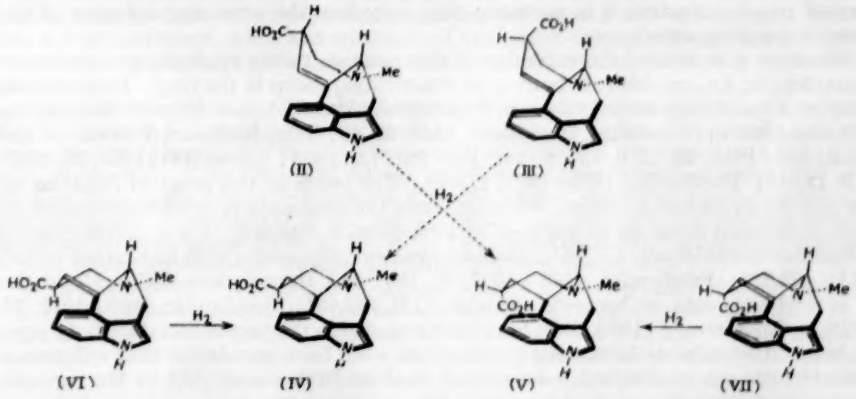


acid I and dihydro*iso*lysergic acid II than in dihydro*iso*lysergic acid I. Thus dihydro*iso*-lysergic acid I should be a stronger base (weaker base-conjugate acid) than the other two isomers. This has now been shown to be correct by measurement of the pK'_a of these three dihydro-acids (see Table). Dissociation constants for dihydrolysergic acid I and

	pK'_a at 20° (present work)	pK'_a at 24° (Craig *et al.*)
Dihydrolysergic acid I	8·50, 8·46	8·45
Dihydro*iso*lysergic acid I	8·88, 8·94	—
Dihydro*iso*lysergic acid II	8·52	8·57, 8·64

dihydro*iso*lysergic acid II measured by Craig *et al.* (*loc. cit.*; they did not give a figure for dihydro*iso*lysergic acid I) agree with ours. The similar values for dihydrolysergic acid I and dihydro*iso*lysergic acid II confirm the similar orientation of the carboxyl group in these acids. The influence of the carboxyl group on the ionisation of the dihydrolysergic acids ($\Delta pK'_{a,2}$ 0·43) is somewhat less than that (0·63) observed by Craig *et al.* for the corresponding lysergic acids and accords with the greater intensity of the direct effect to be expected in the more strongly basic dihydro-derivatives, since with increasing basicity the ionised form becomes more favoured.

Cookson (*loc. cit.*) suggested that ring D in lysergic acid and *iso*lysergic acids has a boat structure. Structures (II) and (III) of this type would, however, lead to the dihydro-acids (V) and (IV) respectively, in each of which the orientation of the carboxyl with



respect to $N_{(6)}$ is the reverse of that in the parent acid. The fact that lysergic and dihydrolysergic acid I are each stronger acids (weaker bases) than their corresponding *iso*-acid (ΔpK values are of the same sign and order of magnitude in each series) implies that the orientation of the carboxyl group relative to $N_{(6)}$ is not significantly altered by hydrogenation of the 9 : 10-double bond. Such a condition is satisfied only if all four acids have identical conformations of ring D (*i.e.*, all either chair or semi-chair) as already postulated (Stenlake, *loc. cit.*). This follows irrespectively of configuration at the new asymmetric centre, $C_{(10)}$. Lysergic and *iso*lysergic acid therefore, have the structures (VI) and (VII) respectively, in which ring D adopts a semi-chair conformation.

[*Added*, December 29th, 1954.]—After submission of this manuscript, Stoll, Petrzilka, Rutschmann, Hofmann, and Günthard (*Helv. Chim. Acta*, 1954, **37**, 2039) reported pK and other evidence leading to similar conclusions with regard to the stereochemistry of lysergic acid and its derivatives.

Experimental.—An alk-acid glass electrode in conjunction with a Pye direct reading pH meter was used for pK determinations. As only 2—3 mg. of material were available the method of Craig *et al.* (*loc. cit.*) was adopted, in which the pK was determined from individual pH measurements at 20° of an 0·002M-solution of the substance, which had been neutralised by the calculated amount of carbonate-free 0·1N-sodium hydroxide. Addition of alkali and dilution to volume were carried out by weight. Control experiments with glycine gave consistent values of pK'_{a_2} 9·80 (Orthner and Hein, *Biochem. Z.*, 1933, **262**, 461, give 9·75; Albert, *Biochem. J.*, 1950, **47**, 531, gives 9·86). The purity of the samples used was confirmed as far as possible by means of their physical constants.

The author thanks Professor A. Stoll for the gift of dihydrolysergic acids, and Dr. A. L. Glenn for helpful discussions and suggestions in the preparation of the manuscript.

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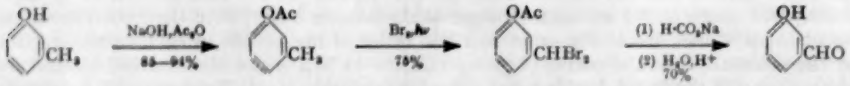
Photobromination Studies. Part II. A Convenient Synthesis of* m-*Hydroxybenzaldehyde.*

By Ernest L. Eliel and Kenneth W. Nelson.

[Reprint Order No. 5986.]

It has recently been found that hydroxybenzaldehydes bearing an electron-withdrawing substituent, such as a nitro-, carboxy-, or methoxycarbonyl group, can be readily synthesized from the corresponding substituted cresols by dibromination of the side-chain followed by hydrolysis (Segesser and Calvin, *J. Amer. Chem. Soc.*, 1942, **64**, 825; Eliel and Rivard, Part I;* Eliel, Rivard, and Burgstahler, *J. Org. Chem.*, 1953, **18**, 1679). To prevent ring-bromination it is necessary only to reduce the activating influence of the phenolic group by acetylation.

We have now studied the extension of this reaction to the synthesis of *m*-hydroxybenzaldehyde, *i.e.*, an aldehyde bearing no deactivating group in the ring. Hitherto, this compound has usually been synthesized by nitration of benzaldehyde followed by reduction and diazotization (Woodward, *Org. Synth.*, 1945, **25**, 55; Icke, Redeman, Wisegarver, and Allen, *ibid.*, 1949, **29**, 72, 6, 63; Kranz, U.S. Pat. 1,715,417; *Chem. Abs.*, 1929, **23**, 3717; G.P. 18,016; Friedlander, 1877—1887, **1**, 586). The yields in this series of reactions are low and the procedure is tedious, especially since the intermediate *m*-aminobenzaldehyde must be handled either as an acetal or as a tin chloride complex. Other preparations of *m*-hydroxybenzaldehyde, *e.g.*, by oxidation of *m*-tolyl sulphonates with manganese dioxide (G.P. 162,322; Friedlander, 1905—1907, **8**, 154) and through side-chain chlorination of *m*-tolyl carbonate or benzoate (Raschig, G.P. 233,631; Friedlander, 1910—1912, **10**, 163; cf. Copisarow, *J.*, 1929, 588), have been reported in the patent literature but appear to be of little value as laboratory preparations. We have now found that *m*-hydroxybenzaldehyde can be obtained from *m*-cresol in about 50% overall yield by the very convenient sequence indicated below:



m-Tolyl acetate, obtained by Chattaway's procedure (*J.*, 1931, 2495) in 85—94% yield, is readily dibrominated photochemically in 75% yield. The hydrolysis of the crude

* Presented before the Division of Organic Chemistry at the 124th Meeting of the American Chemical Society at Chicago, Illinois, September 10th, 1953. Part I, *J. Org. Chem.*, 1952, **17**, 1252.

dibromo-compound was best effected by means of sodium formate (Levene and Walti, *Org. Synth.*, Coll. Vol. II, 1943, 5; Bachmann and Ramirez, *J. Amer. Chem. Soc.*, 1950, **72**, 2525), the yield of aldehyde being 70%.

Some extensions of this reaction to other carbonyl compounds were investigated. The synthesis of *m*-hydroxyacetophenone from the readily available *m*-ethylphenol failed because bromination of the side-chain did not proceed beyond the monosubstitution stage. *p*-Nitrotoluene was dibrominated, and the crude dibromination product hydrolyzed by means of concentrated sulphuric acid (sodium formate was ineffective in this case) to give *p*-nitrobenzaldehyde in rather poor overall yield; a detailed study of this reaction has not been made, however, and it is believed that the yield is susceptible to improvement. *o*-Nitrobenzaldehyde could not be prepared in this manner.

Experimental.—m-*Tolyl acetate.* From 32·4 g. of *m*-cresol, essentially by Chattaway's method (*loc. cit.*), this acetate, b. p. 96·5°/13 mm., was obtained in 85—94% yield (38—42·6 g.).

Photodibromination of m-*tolyl acetate.* A solution of the ester (30 g., 0·2 mole) in carbon tetrachloride (150 ml.), in a two-necked flask equipped with a reflux condenser and dropping-funnel, was illuminated with a 500-w unfrosted tungsten projector bulb. The solution was heated to gentle boiling by means of a small flame, and a solution of bromine (64 g., 0·4 mole) in carbon tetrachloride (225 ml.) was added at such a rate (1¾ hr.) that no permanent red bromine colour appeared in the solution. The solution was then cooled, washed with water, dilute aqueous sodium hydrogen carbonate and again water, dried (Na_2SO_4), and concentrated. Distillation of the residue from a small Claisen flask gave 46 g. (75%) of the crude *m*-acetoxybenzylidene bromide, b. p. 138—147°/1 mm., 165—169°/11 mm. Material so obtained was suitable for the next step.

m-*Hydroxybenzaldehyde.* The following procedure was the best of several studied. To a solution of crude *m*-acetoxybenzylidene bromide (30·8 g., 0·1 mole) in 95% ethanol (150 ml.) was added sodium formate (16·4 g., 0·24 mole); the suspension was then heated to boiling, and enough water (*ca.* 30 ml.) was added to produce a homogeneous mixture. Boiling under reflux was continued for 48 hr. Concentrated hydrochloric acid (*ca.* 5 ml.) was added just before the end of the reflux period. Most of the ethanol was then removed by distillation at reduced pressure, and water was added to bring the total volume to about 50 ml. Upon chilling of the solution in an ice-bath, *m*-hydroxybenzaldehyde was precipitated, and was collected, washed with a little cold water, dried, and recrystallized from ether–light petroleum (b. p. 60—90°). The product so purified (8·5 g., 70%) had m. p. 103—104° (lit. 106°) undepressed by an authentic specimen.

p-*Nitrobenzylidene bromide.* The photobromination of *p*-nitrotoluene (13·74 g., 0·1 mole) in carbon tetrachloride (150 ml.) by bromine (32 g., 0·2 mole) in carbon tetrachloride (150 ml.) appeared to be complete after 3½ hr. The mixture was chilled in ice, diluted with 200 ml. of light petroleum (b. p. 60—90°), and further cooled with carbon dioxide–acetone. The precipitated crude *m*-nitrobenzylidene bromide was collected and washed with a small amount of light petroleum; it weighed 21 g. but was apparently contaminated with the monobromo-compound as shown by the low m. p., 60—65°. Two recrystallizations from ethanol raised the m. p. to 76—78° (Wachendorf, *Annalen*, 1877, **185**, 268, reports m. p. 82°).

p-*Nitrobenzaldehyde.* A well-stirred suspension of *p*-nitrobenzylidene bromide (3·8 g.; m. p. 76—78°) in 45% sulphuric acid (100 ml.) was kept at the b. p. under reflux for 3 hr. It was then exhaustively steam-distilled (about 200 ml. of distillate were collected) and the distillate was warmed to 80°. This dissolved the *p*-nitrobenzaldehyde but left unhydrolyzed dibromo-compound (0·5 g., 11%) as an oil (which crystallized). The hot aqueous phase was decanted and chilled, and the product collected (0·8 g., 42%; m. p. 97·5—100°). Recrystallization from ether–light petroleum did not raise the m. p. above 100—102° (lit., 106·5°), but purification through the bisulphite compound gave material of m. p. 104—106° in 65% yield. The 2 : 4-dinitrophenylhydrazone had m. p. 318° (lit., 320°).

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"*Diazoperbromides.*"

By M. Aroney and R. J. W. Le Fèvre.

[Reprint Order No. 6008.]

Substances corresponding to formulæ RN_2Br_3 were first isolated by Griess (*Annalen*, 1864, **137**, 50; *Phil. Trans.*, 1864, 673; *J.*, 1867, **20**, 36) by the addition of excess of bromine water containing hydrobromic acid to aqueous benzenediazonium nitrate. Subsequent work showed that chlorine, bromine, or iodine could form analogous compounds, and Hantzsch (*Ber.*, 1895, **28**, 2754) prepared trihalides containing nine out of the ten possible combinations of these three halogens.

Griess (*loc. cit.*, 1867, p. 44) remarked "The constitution of the perbromide of diazobenzol appears to be the same as that of periodide of tetraethylammonium and similar compounds of other bases." Chattaway (*J.*, 1909, **95**, 862; 1915, **107**, 105) considered the "diazoperbromides" to be tri-*N*-bromoarylhydrazines ($Ar{\cdot}NBr{\cdot}NBr_2$) because they could be obtained by the direct action of bromine on arylhydrazines. Hantzsch, noting the parallelism between diazoperhalides and perhalides of the alkali metals, concluded (*Ber.*, 1915, **48**, 1344) with Forster (*J.*, 1915, **107**, 260) that the former were true diazonium salts.

Of obvious relevance to this question is the recent observation that a vibration frequency around 2260 cm.$^{-1}$ is characteristic of the $R{\cdot}N_2^+$ cation (Aroney, Le Fèvre, and Werner, *J.*, 1955, 276). We have, therefore, prepared the "diazoperbromides" from *p*-toluidine, *p*-chloroaniline, and β-naphthylamine, and recorded their absorption spectra over the range 3250—1350 cm.$^{-1}$. Results were as tabulated.

Main infrared absorption bands between 3250 *and* 1350 *cm.*$^{-1}$

p-$C_6H_4Me{\cdot}N_2Br_3$	3048	2248	1575	1557		
p-$C_6H_4Cl{\cdot}N_2Br_3$	3072	2250		1555	1465	1410
β-$C_{10}H_7{\cdot}N_2Br_3$	3055	2242	1611			

Reading horizontally, the second feature in each case appeared slightly more intense than the first or third. Two roughly common frequencies are seen, at 3048—3072 and 2240—2250 cm.$^{-1}$. The former, presumably due to C–H stretching vibrations, requires no comment. The latter is well within the limits, *viz.*, 2230—2310 cm.$^{-1}$, found by Aroney *et al.* (*loc. cit.*) to include the "triple bond" absorptions of 21 diazonium salts. We conclude therefore that the perbromides contain the $R{\cdot}N_2^+$ group.

Chattaway (*loc. cit.*) had observed that the oils separating during the preparation of perbromides may hold no fewer than 9 atoms of bromine, although these could only be retained by preventing the escape of bromine vapour. In order to remove the possibility that such higher polybromides contributed to the spectra, and to substantiate that, at the time of recording, the substances were in reality tribromides, bromine estimations were made.

The perbromide (*ca.* 0·3 g.) was dissolved by gentle heat in a solution of sodium sulphite in dilute sulphuric acid, and the mixture refluxed for 10 min. to reduce the bromine to bromide. After cooling, aqueous silver nitrate (0·1N; 50 c.c.) was added with stirring together with nitric acid (6N; 10 c.c.) and ferric alum indicator. Back-titration with standard potassium thiocyanate solution followed. Bromine contents between 1 and 1·5% lower than those calculated for $R{\cdot}N_2Br_3$ were obtained. An estimation without initial reduction indicated an almost total absence of Br^- in the perbromide solution; heating the compounds in dilute acid liberated bromine.

The Br_3^- anion, by analogy with $(ICl_2)^-$ and $(IBr_2)^-$ in salts of the alkali metals, has a rectilinear structure (Mooney, *Z. Krist.*, 1935, **90**, 143; 1938, **98**, 377, cf. Zelezny and Baenziger, *J. Amer. Chem. Soc.*, 1952, **74**, 6151) with the central atom having a *p-d* valency configuration (Kimball, *J. Chem. Phys.*, 1940, **8**, 194). Since $(R{\cdot}N{\vdots}N)^+$ should also be extended, the relative stability of solid diazonium perbromides may, on a simple view, be due to the shapes of their cations and anions which permit a close mutual approach where electrostatic are reinforced by van der Waals forces, thus favouring the stability of an ion-pair arrangement.

University of Sydney, N.S.W., Australia. [*Received, January 4th*, 1955.]

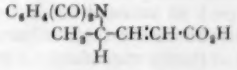
Configuration of (+)-γ-Aminovaleric Acid. Conversion of L-Alanine into its Vinylogue.

By K. Balenović and D. Cerar.

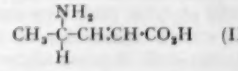
[Reprint Order No. 6018.]

γ-Aminovaleric acid was first prepared and resolved into its optical antipodes by Fischer and Groh (*Annalen*, 1911, **383**, 363) by a very tedious procedure; the (+)- and the (−)-form showed $[\alpha]_D$ +12° and $[\alpha]_D$ −12° in water respectively.

We applied the Doebner condensation (*Ber.*, 1900, **33**, 2140; 1902, **35**, 1137) to L-α-phthaloylimidopropaldehyde, prepared from L-alanine (cf. Balenović, Bregant, Cerar, Fleš, and Jambrešić, *J. Org. Chem.*, 1953, **18**, 297), and obtained the pent-2-enoic acid (I), which after hydrogenation and hydrolysis gave (+)-γ-aminovaleric acid, $[\alpha]_D$ +14°, in an overall yield of 32% (based on L-alanine). (+)-γ-Aminovaleric acid is therefore related to the L-amino-acid series.



(I)



(II)

According to the procedure for the preparation of the vinylogue of glycine (Balenović, Jambrešić, and Urbas, *ibid.*, 1954, **19**, 1589), hydrazinolysis of (+)-4-phthalimidopent-2-enoic (I) at room temperature gave poor yields of (−)-4-aminopent-2-enoic acid (II), the vinylogue of L-alanine.

Experimental.—Proof of configuration of L-α-*phthalimidopropaldehyde.* To a solution of this aldehyde prepared according to Balenović *et al.* (*loc. cit.*) (1 g.; $[\alpha]_D$ −28°) in acetone (10 c.c.), Jones's chromic acid reagent (1·44 c.c.) (Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39) was gradually added at room temperature. The mixture was left for 1 hr. at room temperature, diluted with two volumes of water, and extracted with ether. From the extracts crude *N*-phthaloyl-L-alanine was isolated (1·1 g., 99%), having m. p. 150°, $[\alpha]_D^{19}$ −10·5° ± 0·2° (*c*, 2·0 in EtOH). [Fischer (*Ber.*, 1907, **40**, 489) reported m. p. 150—152° and $[\alpha]_D^{18}$ −17·5°.] It was recrystallized from water for analysis (Found: C, 60·3; H, 4·0. Calc. for $C_{11}H_9O_4N$: C, 60·3; H, 4·1%).

(+)-4-*Phthalimidopent-2-enoic acid* (I). A suspension of the finely powdered aldehyde (2 g., 0·01 mole; $[\alpha]_D$ −28°) and malonic acid (2 g., 0·02 mole) in pyridine (5 g.) was heated for 8 hr. at 70—75° (bath-temp.). The cooled mixture was diluted with five volumes of water, acidified with 10% sulphuric acid to pH 6, and left over-night at 0°. The crystalline *acid* precipitated was collected, washed with 10% sulphuric acid and water, and dried (yield, 2·4 g., 100%). Recrystallization from ethanol gave the pure product (85%), m. p. 163°, $[\alpha]_D^{17}$ +10·5° ± 0·8° (*c*, 1·13 in EtOH) (Found: C, 63·3; H, 4·6. $C_{13}H_{11}O_4N$ requires C, 63·6; H, 4·5%).

(+)-γ-*Phthalimidovaleric acid.* The acid (I) (3 g., 0·01 mole; $[\alpha]_D$ +10°) in ethanol (45 c.c.) was hydrogenated over Adams platinum oxide (100 mg.), 1 mol. being absorbed in 5 hr. The (+)-γ-*phthalimidovaleric acid* precipitated during the hydrogenation was separated by dissolution in hot ethanol (30 c.c.). Evaporation and recrystallization from ethanol gave the pure product (2·9 g., 95%), m. p. 146°, $[\alpha]_D^{17}$ +37·5° ± 0·9° (*c*, 0·3 in EtOH) (Found: C, 63·1; H, 5·4. $C_{13}H_{13}O_4N$ requires C, 63·2; H, 5·3%).

(+)-γ-*Aminovaleric acid.* γ-Phthalimidovaleric acid (2·5 g., 0·01 mole) was heated under reflux during 7 hr. with acetic acid (7 c.c.) and 47% hydriodic acid (8 c.c.), and the mixture left at 0° overnight. Next morning the precipitated phthalic acid was removed, and the filtrate evaporated to dryness under reduced pressure. The residue was again dissolved in water, recovered by evaporation, dissolved in water, and passed through a column containing Amberlite IR-4B (17 g.; 20—50 mesh) at a flow rate of 30 c.c./hr., yielding (+)-γ-aminovaleric acid (1·0 g., 95%), m. p. 202°, $[\alpha]_D$ +9·3°. Recrystallization from water–methanol (1 : 8) gave white prisms of the pure product (0·8 g., 76%), m. p. 208°, $[\alpha]_D^{22}$ +13·9° ± 0·2° (*c*, 0·8 in H_2O). Fischer and Groh (*loc. cit.*) reported m. p. 208°. Paper chromatography on Whatman No. 1 paper, at 19°, with phenol–water as mobile phase and ninhydrin as reagent, gave a violet spot, R_F 0·89 (Found: N, 11·9. Calc. for $C_5H_{11}O_2N$: N, 12·0%).

(−)-4-*Aminopent-2-enoic acid* (II). A solution of (+)-4-phthalimidopent-2-enoic acid (I) (4·2 g., 0·016 mole) in ethanol (24 c.c.) and ethanolic M-hydrazine hydrate (33·6 c.c., 0·016 mole) was stirred at 25° for two weeks. After a few hours separation of phthaloylhydrazine began, which was complete after two weeks. The entire mixture was evaporated to dryness under reduced pressure, and the residue treated with water (45 c.c.) and acidified to pH 5·5 with acetic acid. After 24 hours' stirring at room temperature the phthaloylhydrazine was filtered off (2·1 g., 100%). The filtrate was evaporated to dryness, and a yellow oil remained (2·1 g.) which partly crystallized. This was triturated with water (1 c.c.) and precipitated with ethanol (10 c.c.); white crystals of (−)-4-*aminopent-2-enoic acid* separated [0·23 g., 12%; m. p. 198° (decomp.)]. Recrystallized from water–ethanol, this had unchanged m. p., $[\alpha]_D^{20}$ −4·8° ± 0·9° (*c*, 1·03 in H_2O) (Found: C, 51·7; H, 7·0; N, 12·0. $C_5H_9O_2N$ requires C, 52·2; H, 7·9; N, 12·2%). Paper chromatography of (−)-4-aminopent-2-enoic acid on Whatman No. 1 paper, at 20°, with butanol–water as mobile phase, gave a yellow spot with a ninhydrin solution, becoming violet on standing (R_F 0·08). Phenol–water as mobile phase gave R_F 0·74. An aqueous solution of (−)-4-aminopent-2-enoic acid gave a strong reaction with ninhydrin. The colour was first yellow, then brown, and, on further heating, deep purple.

Preparation of (+)-γ-*aminovaleric acid from* (−)-4-*aminopent-2-enoic acid.* Hydrogenation over Adams platinum oxide (30 mg.) was carried out with a suspension of (−)-4-aminopent-2-enoic acid (86 mg.) in 10% aqueous acetic acid (15 c.c.) at atmospheric pressure and room temperature. After absorption of 1 mol. of hydrogen the catalyst was filtered off, and the filtrate evaporated to dryness under reduced pressure. Partly racemized (+)-γ-aminovaleric acid remained (90 mg., 100%), $[\alpha]_D^{20}$ +5·7° ± 0·6° (*c*, 1·76 in H_2O), the constitution being confirmed by m. p., mixed m. p., and analysis.

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[*Received, January 7th*, 1955.]

Some α-Methylamino-acids.

By K. T. POTTS.

[Reprint Order No. 6019.]

WHEN this research was started structural analogues of the naturally occurring α-amino-acids were being investigated as a source of compounds capable of the inhibition of growth of micro-organisms and it was of interest to study analogues of the amino-acids in which the hydrogen atom on the α-carbon atom had been replaced by a methyl group. A renewed activity in this field has been shown recently (Bergel and Stock, *J.*, 1954, 2409; Jönsson, *Acta Chem. Scand.*, 1954, **8**, 1203, 1211) and our results are now reported.

Experimental.—α-Amino-α-methylglutaric acid (α-methyl-DL-glutamic acid) was synthesised by a method similar to that published recently by Gal, Avakian, and Martin (*J. Amer. Chem. Soc.*, 1954, **76**, 4181) except that inorganic ions were removed from solution by Cocker and Lapworth's method (*J.*, 1931, 1391). It crystallised from water as glistening, white needles, m. p. 175° [Gal *et al.*, *loc. cit.*, report m. p. 168—170° (decomp.)] (Found: N, 8·8. Calc. for $C_6H_{11}O_4N$: N, 8·7%). The *phthaloyl* derivative (method: Billman and Harting, *J. Amer. Chem. Soc.*, 1948, **70**, 1473) formed white platelets (from water), m. p. 203° (Found: C, 57·9; H, 4·5. $C_{14}H_{13}O_6N$ requires C, 57·8; H, 4·5%).

α-Amino*iso*butyric acid (α-methyl-DL-alanine) was prepared by the alkaline hydrolysis of 5 : 5-dimethylhydantoin (Bucherer, *J. pr. Chem.*, 1934, **141**, 28). It crystallised from water as white needles and sublimed at 280° without melting (Found: C, 46·5; H, 8·6. Calc. for $C_4H_9O_2N$: C, 46·6; H, 8·8%). Urech (*Annalen*, 1872, **164**, 268) also reported that it sublimed at 280° without melting.

α-*Methyl*-DL-*phenylalanine.* 5-Benzyl-5-methylhydantoin (30 g.; Bucherer, *loc. cit.*), barium hydroxide (150 g.), and water (750 c.c.) were boiled under reflux for 30 hr. After removal of barium ions as barium carbonate and concentration of the mother-liquor, α-methyl-DL-phenylalanine (14 g., 53%) separated as white needles, m. p. 294—295° (decomp.) (Herbst

and Johnson, *J. Amer. Chem. Soc.*, 1932, **54**, 2463, report m. p. 293—294° with charring) (Found : C, 67·1; H, 7·2; N, 7·8. Calc. for $C_{10}H_{13}O_2N$: C, 67·0; H, 7·3; N, 7·8%).

α-*Methyl*-DL-*methionine*. (*a*) 5-Methyl-5-(methylthioethyl)hydantoin. Methyl 3-oxobutyl sulphide (8·0 g.) (Gill, James, Lions, and Potts, *ibid.*, 1952, **74**, 4927) in 50% alcohol (60 c.c.), potassium cyanide (6·4 g.), and ammonium carbonate (20 g.) were heated together at 65—70° for 3 hr. The solution was evaporated to dryness (reduced pressure, water-bath) and the residue extracted several times with hot benzene. The *hydantoin* (3·5 g., 28%) crystallised from the benzene solution. It was soluble in alcohol, acetone, water, and hot benzene and crystallised from benzene as white, irregular prisms, m. p. 108° (Found : C, 44·9; H, 6·7; N, 14·8. $C_7H_{12}O_2N_2S$ requires C, 44·7; H, 6·4; N, 14·9%). (*b*) α-Methyl-DL-methionine. 5-Methyl-5-(methylthioethyl)hydantoin (3·2 g.), barium hydroxide (20 g.), and water (100 c.c.) were refluxed together for 36 hr. and the mother-liquor treated as in the previous hydrolyses. After several days, *α-methyl-*DL-*methionine* (0·9 g., 32%) separated as white needles, m. p. 134°, and crystallised from water as white needles without rise in m. p. (Found : S, 19·4. $C_6H_{13}O_2NS$ requires S, 19·6%).

α-*Methyl*-DL-*tyrosine*. (*a*) 5-4′-Methoxybenzyl-5-methylhydantoin. *p*-Methoxyphenylacetone (28 g.) (Hoover and Haas, *J. Org. Chem.*, 1947, **12**, 501), potassium cyanide (15 g.), and ammonium carbonate (50 g.) in 50% alcohol (250 c.c.) were heated together at 65—70° for 7 hr. After cooling, the mixture set to a crystalline mass of the *hydantoin* (38·5 g., 97%); a further quantity was isolated from the mother-liquor by the careful addition of hydrochloric acid. It crystallised as fine, white needles, m. p. 198°, from water (Found : C, 61·5; H, 6·2; N, 12·2. $C_{12}H_{14}O_3N_2$ requires C, 61·5; H, 6·0; N, 12·0%). (*b*) 5-4′-Hydroxybenzyl-5-methylhydantoin. The above hydantoin (33·5 g.) and hydriodic acid (150 c.c.; *d* 1·7) were heated together for 30 min. Methyl iodide was rapidly evolved and *5-4′-hydroxybenzyl-5-methylhydantoin* (30 g., 94%) separated from the hot mixture. It crystallised from water as white needles, m. p. 307° (decomp.) (Found : C, 60·0; H, 5·5; N, 12·8. $C_{11}H_{12}O_3N_2$ requires C, 60·0; H, 5·5; N, 12·7%). (*c*) α-Methyl-DL-tyrosine. 5-4′-Hydroxybenzyl-4-methylhydantoin (20 g.) was hydrolysed with barium hydroxide (100 g.) in water (500 c.c.) and the mixture worked up as above. *α-Methyl-*DL-*tyrosine* (6·2 g., 35%) crystallised from water as white, irregular prisms, m. p. 330—332° (decomp.) (Found : C, 61·2; H, 6·7; N, 7·5. $C_{10}H_{13}O_3N$ requires C, 61·6; H, 6·7; N, 7·2%).

α-*Methyl*-DL-*di-iodotyrosine*. A solution of iodine in 4N-potassium iodide (10·4 c.c.) was added slowly and with shaking to a solution of α-methyltyrosine (2·0 g.) in water (20 c.c.) and an excess of 60% aqueous ethylenediamine. After 2 hr. at room temperature the mixture was neutralised with acetic acid and, after a period, pale yellow crystals (3·8 g., 85%) separated. *α-Methyl-*DL-*di-iodotyrosine* crystallised from 50% aqueous acetic acid as fine, white needles, m. p. 215° (decomp.) (Found : C, 27·2; H, 3·0; N, 3·3 $C_{10}H_{11}O_3NI_2$ requires C, 26·9; H, 2·5; N, 3·1%).

S-*Benzyl-α-methyl-*DL-*cysteine*. (*a*) 5-(4-Methylthiobenzyl)-5-methylhydantoin. 1-(Benzylthio)acetone (100 g.) (Wahl, *Ber.*, 1922, **55**, 1449), potassium cyanide (48 g.), and ammonium carbonate (162 g.) in 50% alcohol (400 c.c.) were heated together at 65—70° for 7 hr. The solution was then concentrated (reduced pressure, water-bath) and poured on cracked ice; careful addition of dilute hydrochloric acid caused complete precipitation of the *hydantoin* (128 g., 92%). It crystallised from alcohol as white needles, m. p. 119° (Found : C, 57·7; H, 5·6; N, 10·9. $C_{12}H_{14}O_2N_2S$ requires C, 57·6; H, 5·6; N, 11·2%). (*b*) *S*-Benzyl-α-methyl-DL-cysteine. The above hydantoin (50 g.), barium hydroxide (250 g.), and water (1250 c.c.) were heated under reflux for 30 hr. Barium ions were precipitated as barium carbonate from the solution at 100° and, after cooling, S-*benzyl-α-methyl-*DL-*cysteine* (34·8 g., 71%) crystallised as white needles, m. p. 234°. The m. p. was not raised on further recrystallisation (Found : C, 58·2; H, 6·7; N, 6·4; S, 13·9. $C_{11}H_{15}O_2NS$ requires C, 58·6; H, 6·7; N, 6·2; S, 14·3%).

5-(4-Hydroxy-3 : 5-dinitrobenzyl)-5-methylhydantoin. 5-4′-Hydroxybenzyl-5-methylhydantoin (10 g.) was added in small quantities during 90 min. to a stirred solution of concentrated nitric acid (35 c.c.; *d* 1·42), at 25—32°. During 30 min. a solid separated and the mixture was then poured on cracked ice. The *dinitrohydantoin* (10·5 g., 75%) crystallised from water as yellow needles, m. p. 273° (decomp.) (Found : C, 42·8; H, 3·4; N, 18·1. $C_{11}H_{10}O_7N_4$ requires C, 42·6; H, 3·3; N, 18·1%).

The nitro-compound (5 g.), toluene-*p*-sulphonyl chloride (4·6 g.), and dry pyridine (40 c.c.) were heated under reflux for 30 min. *p*-Methoxyphenol (6·8 g.) was then added and the whole heated for a further 2 hr. The pyridine was removed under reduced pressure, the residual oil dissolved in acetone, and the solution poured on cracked ice. The precipitated solid (4·6 g., 69%)

crystallised first from dilute acetone and then from methanol and 5-(4-p-*methoxyphenoxy*-3 : 5 *dinitrobenzyl*)-5-*methylhydantoin* was obtained as pale yellow needles, m. p. 147° (Found : N, 13·0. $C_{18}H_{16}O_8N_4$ requires N, 13·4%).

I thank Dr. F. Lions for encouragement and advice.

THE UNIVERSITY OF SYDNEY, AUSTRALIA.
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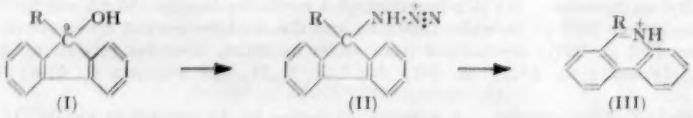
[*Received, January 8th*, 1955.]

Reactions of Organic Azides. Part IV. The Conversion of 9-Alkylfluoren-9-ols into 9-Alkylphenanthridines.*

By C. L. ARCUS and E. A. LUCKEN.

[Reprint Order No. 6021.]

IT has been found (Parts I and III *) that fluoren-9-ols react with hydrazoic acid in the presence of sulphuric acid to yield phenanthridines. The mechanism of the reaction has been discussed (*locc. cit.*) : the essential step is the rearrangement of a protonated azide (II) to a phenanthridinium ion (III), and it has been shown, from the results with 2- and 3-substituted fluoren-9-ols, that the relative migratory aptitudes of the two rings in such a fluorenol are directly related to the capacities of the rings for electron-release at their point of attachment to $C_{(9)}$.



The effect on the course of the reaction of electron-release at $C_{(9)}$ by the group R (in I) (*i.e.*, release other than by the migrating rings) has now been investigated. 9-Ethyl-, 9-*iso*propyl-, and 9-*tert.*-butyl-fluoren-9-ol have been converted into the corresponding 9-alkylphenanthridines; the yields (at 25°, total reaction time 2¼ hours) are recorded in the Table. Inductive electron-release increases, and release by hyperconjugation decreases,

Phenanthridine :		9-Ethyl-	9-*iso*Propyl-	9-*tert.*-Butyl- *
Yield (%)	Expt. (i)	84	79	66
	Expt. (ii)	89	88	61

* 9-Azido-9-*tert.*-butylfluorene, (i) 19, (ii) 21%, also isolated.

in the series ethyl, *iso*propyl, *tert.*-butyl. The yield of 9-methylphenanthridine from 9-methylfluoren-9-ol has been found (Part III) to be 47% under similar conditions (time : 2 hours) ; however, this value cannot properly be compared with those in the Table, because methylfluorenylmethylphenanthridine was also formed, in 27% yield, a side-reaction not encountered with the other 9-alkylfluoren-9-ols.

From the reaction with 9-*tert.*-butylfluoren-9-ol, as from that with unsubstituted fluoren-9-ol (Part I), the intermediate azide was isolated. It is inferred, at least for these two fluorenols, that the last of the following reactions is rate-controlling :

$$R'OH + 2H_2SO_4 \longrightarrow R'^{+} + H_3O^{+} + 2HSO_4^{-}$$

$$R'^{+} + HN_3 \longrightarrow R'\cdot\overset{+}{N}_3H$$

$$R'\cdot\overset{+}{N}_3H \longrightarrow R'\overset{+}{N}H + N_2$$

The comparatively low yield of 9-*tert.*-butylphenanthridine is therefore ascribed to the relatively slow decomposition of the protonated azide. Decomposition results in the

* Part I, *J.*, 1953, 178; Part III, *J.*, 1954, 4319.

formation of the $R\overset{+}{C}{=}\overset{\diagdown}{N}H$ double bond (which may alternatively be regarded as the aromatisation of the central ring), a process which would be expected to be facilitated by hyperconjugation with R; hyperconjugation is possible with ethyl and *iso*propyl, but not with *tert.*-butyl. A result relating to the effect of conjugation by R has been recorded in Part III: 9-phenylfluoren-9-ol, on reaction as above, but for 2 hours, gave 9-phenylphenanthridine in 94% yield; the phenyl group is presumed to conjugate with the heterocyclic ring as the latter is formed.

It is concluded that a capacity for hyperconjugation or conjugation by the group R facilitates, but is not essential to, the rearrangement of the protonated azide to the phenanthridinium ion.

Experimental.—A solution of fluorenone (11·2 g.) in benzene–ether (25 ml. each) was added to ethylmagnesium bromide [from magnesium (1·92 g.), ethyl bromide (5·8 ml.), and ether (70 ml.)] during 1 hr.; the whole was heated under reflux for a further hour, and, when cold, was added to a mixture of ice and ammonium chloride. Benzene (200 ml.) was added, the whole was shaken, and the organic layer separated. The latter was washed with water and then dried (Na_2SO_4), and the solvents were distilled; the product, on recrystallisation from light petroleum (b. p. 60—80°), yielded 9-ethylfluoren-9-ol (7·4 g.), m. p. 99—100°, and m. p. 101° on further recrystallisation. Ullmann and von Wurstemberger (*Ber.*, 1905, **38**, 4107) record m. p. 101°.

A similar preparation with fluorenone (10·8 g.) and *iso*propylmagnesium bromide [from magnesium (2·10 g.) and *iso*propyl bromide (7·4 ml.)] yielded 9-*iso*propylfluoren-9-ol (6·1 g.), m. p. 119—121°, and m. p. 127° after repeated recrystallisation from light petroleum (b. p. 100—120°). Schlenk and Bergmann (*Annalen*, 1928, **463**, 214) record m. p. 124°.

A similar preparation with fluorenone (18·0 g.) and *tert.*-butylmagnesium chloride [from magnesium (4·6 g.) and *tert.*-butyl chloride (21·8 ml.)] gave 9-tert.-*butylfluoren*-9-*ol* [4·0 g., from light petroleum (b. p. 100—120°)], m. p. 80—90°, which formed prisms, m. p. 96°, on repeated recrystallisation from light petroleum (b. p. 40—60°) (Found: C, 86·1; H, 7·9. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%).

To a suspension of sodium azide (2·0 g.) in chloroform (20 ml.), cooled in ice, sulphuric acid (97%; 8 ml.) was added with stirring during ½ hr. The ice was replaced by a water-bath at 25°, and a solution of 9-ethylfluoren-9-ol (4·20 g.) in chloroform (10 ml.) was added during 1½ hr.; stirring was continued for 1 hr. The mixture was poured into cold water (300 ml.); the chloroform layer was extracted with dilute hydrochloric acid, and the extract added to the main acidic solution. The combined aqueous solutions were made alkaline with sodium hydroxide solution, and the precipitated base was extracted with ether. The extract was dried (Na_2SO_4) and the ether was distilled; there was obtained 9-ethylphenanthridine (3·58 g.), m. p. 50—53°. In a similar experiment the fluorenol (2·10 g.) yielded the base (1·84 g.). 9-Ethylphenanthridine, recrystallised from acetone, had m. p. 55·5°, and formed a *picrate*, golden needles (from dioxan), m. p. 211° (decomp.) (Found: N, 12·6. $C_{21}H_{16}O_7N_4$ requires N, 12·85%); Pictet and Hubert (*Ber.*, 1896, **29**, 1186) record m. p. 54—55° for the base.

By the same procedure 9-*iso*propylfluoren-9-ol [4·48 g., added in solution in chloroform (25 ml.)] gave 9-iso*propylphenanthridine* (3·47 g.), m. p. 50—53°. In a similar experiment the fluorenol (2·24 g.) yielded the base (1·98 g.). After recrystallisation from aqueous ethanol, 9-*iso*propylphenanthridine formed needles, m. p. 55° (Found: C, 86·9; H, 6·9; N, 6·35. $C_{16}H_{15}N$ requires C, 86·8; H, 6·85; N, 6·35%) [*picrate*, yellow prisms (from dioxan), m. p. 206° (decomp.) (Found: N, 12·3. $C_{22}H_{18}O_7N_4$ requires N, 12·45%)].

Finely powdered 9-*tert.*-butylfluoren-9-ol [(i), (ii) 2·40 g.] was added with stirring during ¾ hr. to a hydrazoic–sulphuric acid solution [prepared as above from sodium azide (1·0 g.), chloroform (15 ml.), and sulphuric acid (4 ml.)] kept at 25°; stirring was continued for 1¼ hr. The chloroform layer was decanted and extracted with 10N-sulphuric acid. The extract was added to the sulphuric acid layer, which had been diluted with 150 ml. of water; the whole was then made alkaline and extracted as described above. The base so obtained [(i) 1·58, (ii) 1·45 g.] was an oil which on distillation (b. p. > 250°/5 mm.) yielded 9-tert.-*butylphenanthridine* (Found: C, 86·9; H, 6·85; N, 5·7. $C_{17}H_{17}N$ requires C, 86·8; H, 7·3; N, 5·95%); it separated from ethanol as buff prisms, m. p. 74° [*picrate*, yellow prisms (from dioxan), m. p. 212° (decomp.) (Found: N, 12·0. $C_{23}H_{20}O_7N_4$ requires N, 12·1%)]. Evaporation of the chloroform solution gave 9-*azido*-9-tert.-*butylfluorene* [(i) 0·50, (ii) 0·57 g.], m. p. 66—68°, which on recrystallisation from acetone

formed prisms, m. p. 69° (Found: C, 77·6; H, 6·5; N, 16·3. $C_{17}H_{17}N_3$ requires C, 77·6; H, 6·45; N, 16·0%).

Thanks are expressed to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Limited for grants, and to the Department of Scientific and Industrial Research for a maintenance grant (to E. A. L.).

BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, January 10th*, 1955.]

The Decomposition of Cystine in Acid Solution in the Presence of Indoles.

By J. T. EDWARD and E. F. MARTLEW.

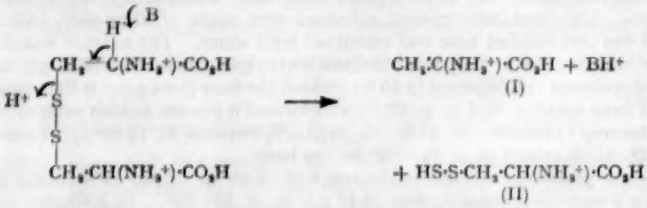
[Reprint Order No. 6060.]

OLCOTT AND FRAENKEL-CONRAT (*J. Biol. Chem.*, 1947, **171**, 583) found that cystine in 7N-hydrochloric acid containing tryptophan at 110° afforded cysteine in about 25% yield. The other naturally occurring amino-acids were without effect. This reaction is of some importance in the hydrolysis of proteins, such as chymotrypsinogen (Brand and Kassel, *J. Gen. Physiol.*, 1941, **25**, 167) and lysozyme (Olcott and Fraenkel-Conrat, *loc. cit.*), which contain large amounts of tryptophan.

We have found that the formation of cysteine is catalysed by other indoles besides tryptophan, and by xanthhydrol, but not by diphenylamine. Examination of the reaction products by paper chromatography showed several other ninhydrin-positive compounds to be formed with cysteine; two of them appeared to be serine and alanine, from their R_F values in three different solvent systems.

Alanine and serine, along with ammonia, pyruvic acid, cysteic acid, hydrogen sulphide, and sulphur, are formed by the decomposition of cystine in phosphoric acid at 100° (Andrews and Bruce, *Arch. Biochem. Biophys.*, 1951, **33**, 427).

It is likely that these decompositions are acid–base-catalysed reactions as shown, the intermediate (I) leading to serine, alanine, or pyruvic acid and ammonia by hydration, reduction, or hydrolysis respectively, and the intermediate (II) to cysteine, sulphur,



cysteic acid, or hydrogen sulphide. The base (B) would be the indole-nitrogen or the $H_2PO_4^-$ or HPO_4^{2-} ions. This would explain why acids stronger than phosphoric are ineffective, the anions derived from them being too weak as bases; and why bases stronger than indole are ineffective in 7N-hydrochloric acid, being completely protonated in acid of this strength. Tarbell and Harnish (*Chem. Rev.*, 1951, **49**, 1) have advanced a similar mechanism for the hydrolysis of cystine to cysteine and other products by aqueous alkali.

Experimental.—Chromatographic identification of cysteine. *N*-Phenylmaleinimide, like *N*-ethylmaleinimide (Hanes, Hird, and Isherwood, *Nature*, 1950, **166**, 288), reacted within a few minutes with cysteine to give a compound (CYS–NPM) which travelled as a compact spot on paper chromatograms, the R_F values for three different solvents being shown in the Table. When phenol–water was used as the developing solvent, the compound failed to give a ninhydrin-positive spot on the chromatogram. The preparation of *N*-phenylmaleinimide (Anschutz and Wirtz, *Annalen*, 1887, **239**, 137) is considerably easier than that of the *N*-ethyl analogue.

Chromatographic analysis of products from cystine. Cystine (10 mg.) and the indole or other base (10 mg.) were heated to 100° in 7N-hydrochloric acid (1 ml.) for 18 hr. in a sealed tube. The mixture was taken to dryness and dissolved in a little water, and the process repeated twice to remove hydrochloric acid as completely as possible. The residue was dissolved in 75% aqueous ethanol (1 ml.) containing 50 micromoles of *N*-phenylmaleinimide, and portions (3 and 6 μl.) were spotted on Whatman No. 1 filter-paper chromatograms. Development was carried out by the ascending technique using as solvents: (A) butanol–acetic acid–water (4 : 1 : 5 v/v); (B) propanol–water (7 : 3 v/v); (C) butanol saturated with water. The R_F values of the ninhydrin-positive spots ("Prod.") given by the reaction of cystine in the presence of 2-methylindole are tabulated below, together with the R_F values of known amino-acids ("Std.") run as standards on the same chromatogram.

	Solvent A		Solvent B		Solvent C	
	Std.	Prod.	Std.	Prod.	Std.	Prod.
Cystine	0·04	0·03	0·08	0·11	0·00	0·00
Serine	0·09	0·10	0·26	0·29	0·02	0·03
Alanine	0·18	0·20	0·32	0·33	0·04	
CYS·NPM	0·41	0·39	0·51	0·52	0·17	0·15
Unidentified	—	0·25, 0·47	—	0·41	—	0·23
	—	0·52, 0·58	—	0·63	—	0·34

Cystine was decomposed to the same products when heated in the presence of tryptophan or xanthhydrol. However, indole and 1 : 2 : 3 : 4-tetrahydrocarbazole did not catalyse the decomposition in 7N-hydrochloric acid, although they did in a mixture of 11N-hydrochloric acid (0·7 ml.) and acetic acid (0·4 ml.); this may be due to their negligible solubility in the first medium or to the greater acidity of the second. The catalytic activity of skatole, 2-methylindole, and tryptophan, but not of diphenylamine, was demonstrated in the second medium.

We are grateful to Professor M. Stacey, F.R.S., for encouragement and advice, to the University of Birmingham for an I.C.I. Research Fellowship (to J. T. E.), and to the Department of Scientific and Industrial Research for a maintenance grant (to E. F. M.).

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, January 24th*, 1955.]

OBITUARY NOTICES.

FREDERIC LEATHLEY GOODALL.

1902—1954.

F. L. Goodall was a Yorkshireman—a fact of which he was very proud—being a native of Leeds and receiving his education at Leeds Grammar School and at Leeds University. He graduated B.Sc., with first-class honours in colour chemistry, in 1922, and was awarded a Clothworkers' Research Scholarship. For the next year he worked in collaboration with the late Professor A. G. Perkin and, with him, published in the *Journal* a paper on "Some Reduction Products of Hydroxyanthraquinones."

In 1923 he accepted a position as chemist with C. R. Roberts & Co. Ltd., who were then the Geigy agents for Yorkshire, and later, on the formation of the Geigy Colour Co. Ltd., he became chief chemist and subsequently Yorkshire Area Manager. In 1948 he migrated to Manchester and became Sales Director of the Geigy Company Limited, and was nominated Joint Managing Director in March 1953. In all these capacities, to use the words of the Chairman of the Geigy Company, "he diligently applied his great knowledge of the tinctorial arts, and also inspired all those responsible to him with his leadership."

On behalf of the Company he visited Australia and America, and particularly in the latter country his technical abilities and wide knowledge of dyeing were appreciated in many quarters. No reference to F. L. Goodall would be complete without placing on record the high esteem in which he was held throughout the Geigy organisation in Basle, his knowledge and experience, in particular in the wool field, being recognised and fully appreciated. His excellent knowledge of German was but one weapon in his armoury which proved of great value in his international contacts.

Outside his family life and his business contacts, his main interest had been the Society of Dyers & Colourists, of which he had been a member since 1921, when he joined the Leeds Junior Branch. His election to the Presidency was regarded as a natural and fitting climax to many years of devoted service. During the brief period in which he held office, he looked upon his position as one to be fulfilled at all costs, and those who knew him intimately realised that on many occasions these responsibilities were upheld in spite of difficulties experienced through ill-health. Goodall was a member of the Textile Industries & Dyeing Committee, Leeds University, the Chemistry Sectional Committee, Manchester College of Technology, and the Society of Chemical Industry, Manchester Section.

In his younger days, Goodall was a keen rugby player and was for some time secretary and vice-captain of the Old Leodensians' Rugby Team. He was skilled in the use of the foils and won the fencing championship of Leeds University. In more recent years he was a keen golfer and fisherman, and an inveterate reader.

In his business career he functioned in many rôles—scientist, technician, and administrator—but that in which he will be best remembered is one which he filled with charm and understanding—the rôle of "guide, philosopher, and friend."

J. Holt.

BERNARD MOUAT JONES.

1882—1953.

Bernard Mouat Jones was born in London in 1882, the fourth son of Alexander Mouat Jones. He was educated at Dulwich College and Balliol College, Oxford, where he obtained a First Class in the Final Honours School of Natural Science in Chemistry and also First Classes in Mineralogy and Crystallography. He took his B.A. in 1905 and his M.A. in 1908.

In 1905 he became Research Assistant in Mineralogical Chemistry at the Imperial Institute and the following year was appointed Professor of Chemistry at the Government College, Lahore. He returned in 1913 to become Assistant Professor of Chemistry at the Imperial College of Science and Technology, S. Kensington, and was also made Warden of the University Hall of Residence, Chelsea.

On the outbreak of war (1914) he enlisted as a private in the London Scottish Regiment and the following year was promoted to Captain and Assistant Director, Central Laboratory, G.H.Q., France. Here he was engaged in a great variety of problems including the study of poison gases and among other achievements he succeeded in identifying mustard gas after its use by the enemy.

He was awarded the D.S.O. in 1917, was promoted to Major and then to Lieut.-Colonel and Director of the Central Laboratory in 1918, and was thrice mentioned in despatches.

In 1919 he was appointed Professor of Chemistry and Director of the Edward Davies Chemical Laboratories at the University College of Wales, Aberystwyth. There was at this time a great influx of ex-service men which strained the resources of his department to the utmost but, thanks largely to his great administrative ability, his tireless devotion to the task, and his cheerful and encouraging leadership, the demand was fully met. During this time also he was responsible for revising and editing the sixth edition of Roscoe and Schorlemmer's standard text-book on Inorganic Chemistry.

In 1921 he was appointed Principal of the College of Technology, Manchester, and Dean of the Faculty of Technology in the University of Manchester. He came after a period of discord resulting from the complexity of the affairs and government of the College. It required a man of his great courage, his superb tact, his wide knowledge, his honesty of purpose, and his gentlemanly approach to handle a difficult situation, and he did so with outstanding success. The seventeen years he was at the College were marked by harmony, goodwill, and great progress. He enhanced its reputation and left it a highly esteemed institution in the academic and industrial life of the area and a great centre of higher technological education.

During this time his great energy and capabilities found expression in other spheres. He was a member of the Committee on Higher Technological Education, of the Committee on Higher Commercial Education, of the Advisory Committee on Education in the Colonies, and of the Makerere-Khartoum Education Commission (1937). He was Chairman of the Association of Principals of Technical Institutions, Chairman and later (1943) President of the Association of Technical Institutions. He became President of the Manchester Literary and Philosophical Society (1930) and Chairman (1936—1939) of the Northern Branch of the National Library for the Blind.

He succeeded the late Sir James Baillie as Vice-Chancellor of Leeds University in 1938. It was typical of the modesty and selflessness of the man that, on the outbreak of war the following year, he joined the local Home Guard, later becoming its gas officer with the rank of Lieutenant. For six months in 1941 he was Chief Superintendent of the Chemical Warfare Research Station.

Having successfully guided the University through the difficult war years, he was faced with the problem of dealing with the greatly increased intake of students which followed and his skilful planning enabled the University to double the number of admissions.

During his time at Leeds he was a member of the Commission on Higher Education in West Africa (1944) and he was made an Honorary Freeman of the Company of Clothworkers.

Since practically his whole life since 1914 was devoted to administration, his output of scientific work was not large. There were two papers in 1906 on minerals, and five on the spontaneous crystallization of solutions, in the *Journal* between 1908 and 1913, and one also in the *Journal* on the dissociation of gaseous nitrogen trioxide in 1914.

His contribution to the cause of science was destined to be made not so much in the magnitude of his own researches as in the provision of the opportunities of learning for others in ever increasing numbers.

The conferment of the honorary degrees of LL.D. (Wales), LL.D. (Leeds), and D.C.L. (Durham) was a token of the very high regard in which he was held and of his great achievements.

He had a great sense of humour and a ready wit. There will ever remain in the memory of those who knew him the brilliance of his speeches. He had the gift of applying a good story to illustrate and drive home each point, and his oratory had a sparkle which delighted his audience. His style of delivery gave no indication of the infinite pains which he undoubtedly took in preparation.

He was a bachelor and on retirement went to live with his sister at Rowledge, near Farnham, Surrey, where he died on September 11th, 1953.

O. Rhys Howell.

HARRY GORDON REEVES.

1896—1952.

Gordon Reeves, Senior Lecturer in Biochemistry at the Medical College of St. Bartholomew's Hospital, was a man whose whole professional life was devoted to the teaching of biochemistry. He was one of that now fairly small group of graduates in chemistry who entered biochemistry through a post in a Department of Physiology in a large Medical School, an experience and

training which admirably equip a man for the teaching of what might be termed Medical Biochemistry. Throughout his early career Reeves held posts which entailed heavy and extremely varied teaching duties, but through this general experience he acquired a knowledge of most aspects of physiology which later proved invaluable to him as a teacher of biochemistry.

He entered Birmingham University in October, 1914, after early education at the Central Secondary School, Suffolk Street, Birmingham, and during his degree course in chemistry he assisted in war work carried out for a Government Department. He took his B.Sc. in 1919, B.Sc. (Hons. Chem.) in 1920, and M.Sc. in 1922. He was awarded his Ph.D. in Chemistry in 1925 after research, under Professor P. F. Frankland, F.R.S., on problems concerned with the testing of tar and benzene. In 1928 he was awarded his D.Sc.

As a student, and indeed throughout his whole career, he had a great interest in student organisations. At Birmingham he gave unsparing service to the Guild of Undergraduates, first on the Committee, then as Treasurer, and finally as President. Other student societies also received his allegiance and support, including those concerned with chemistry, drama, debating, and music, and his enthusiasm and unselfishness made him a highly valued and popular member of the student fraternity. These interests he maintained throughout his whole life, and it is also of interest that he never lost his love for Birmingham. Almost every year he spent a considerable part of his summer holiday with his relatives in that city.

Reeves's professional career can be divided into two distinct parts. The first started with his appointment as Assistant Lecturer and Demonstrator in Biochemistry at King's College, London, in 1923, and continued when he was Demonstrator in the Department of Physiology at the Medical College of St. Bartholomew's Hospital (1926—1936). During this period his heavy teaching duties left him few opportunities for research, but nevertheless he made useful contributions to our knowledge of the metabolism of carbohydrate in muscle and other tissues, with papers published in the *Biochem. J.*, *J. Physiol.*, *Quart. J. exp. Physiol.*, and this *Journal*. He was particularly interested in dihydroxyacetone and glyceraldehyde as possible intermediary products in the metabolism of glucose, and he also collaborated in investigations on the factors which are concerned with the clotting of blood.

It was during the second phase of his service at "Barts", starting in 1936 with his transference to the newly created Department of Biochemistry and Chemistry, that Reeves grew to full stature as a university teacher. Promotion came fairly rapidly. After a short period as demonstrator, he became lecturer and then senior lecturer in biochemistry—a well-deserved recognition of good work he did during the war-time housing of the Preclinical School of St. Bartholomew's Hospital Medical College at Cambridge, and the post-war period of rehabilitation and expansion in Charterhouse Square.

Reeves was an excellent teacher of the fundamentals of biochemistry in relation to medicine, and he was well equipped, and always quite willing, to lecture at very short notice on any aspect of 2nd M.B. organic chemistry and biochemistry. Many hundreds of students who have passed through the preclinical school at Barts have good reason to be grateful to him. Senior teachers who possess this versatility and this enthusiasm for teaching are comparatively rare, and their contribution, direct and indirect, to the advancement of their particular subject should not be underestimated.

Gordon Reeves was a well-loved and deservedly popular member of the staff of the Department of Biochemistry at Barts. His students liked and respected him, delighting in his occasional mannerism or idiosyncrasy. Outside his work he found abundant and lasting pleasure in music and the theatre. Here again, his versatility was very evident, for besides being a keen musician and vocalist he had considerable dramatic ability and the capacity to give expert advice on the production of plays. In particular, he had a great love for, and wide knowledge of, the Gilbert and Sullivan operas.

In recent years Reeves had developed a bronchitis which caused him considerable discomfort and ill health, particularly during the winter, and this illness ultimately brought about his death on November 22nd, 1952, at the age of 56. Even during his long period of ill health he retained his happy nature, and his colleagues will for ever remember him for his cheerful smile, his good humour, and his willingness to carry out, loyally and unselfishly, any task which might help his colleagues and his students.

A. WORMALL.

THE CHEMICAL SOCIETY

'SPECIAL PUBLICATION' NO. 2

PEPTIDE CHEMISTRY

The following Papers, presented at a Symposium held on March 30th, 1955, will shortly be published with a report of the discussion as No. 2 in the Society's series of "Special Publications."

1. "Deuterium Exchange between Peptides and Water," by K. Linderstrøm-Lang (Carlsberg Laboratorium, Copenhagen).

2. "New Aspects of the Chemistry of Peptide Synthesis from *N*-Carboxy-α-amino acid Anhydrides," by C. H. Bamford (Courtaulds Ltd., Maidenhead).

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